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Southwest Allergy Forum

INTRODUCTION

THE SOUTHWEST Allergy Forum began its existence as the Texas Allergy Association. Through the efforts of Dr. Maurice Barnes, the allergists of Texas were first assembled for dinner during the 1938 meeting of the Texas State Medical Association in Galveston. Then in April, 1939, the Texas Allergy Association was founded during discussions in the room of Dr. Homer Prince at the Guenther Hotel in San Antonio.

A meeting of this group was held in 1940, but in 1941 in Fort Worth the name was changed to the "Southwest Allergy Forum." Members were accepted from a large number of states, and at the present time the Forum is almost national in its scope and has a membership of two hundred. One of the distinguishing features of the group has always been its lack of formality, and the welcoming of informal discussions from the floor. This has encouraged the younger allergists to take an active part in the proceedings.

Meetings of a high calibre have been held each year in the following cities: 1940—Dallas, Texas; 1941—Fort Worth, Texas; 1942—Little Rock, Arkansas; 1943—Dallas, Texas; 1944—Jackson, Mississippi; 1945—New Orleans, Louisiana; 1946—Houston, Texas; 1947—Shreveport, Louisiana; 1948—Oklahoma City, Oklahoma; 1949—El Paso, Texas; 1950—Memphis, Tennessee; 1951—San Antonio, Texas; 1952—Dallas, Texas; 1953—Kansas City, Missouri; and 1954—New Orleans, Louisiana.

The 1955 meeting will be held in Little Rock, Arkansas, January 9 through 11, at the Marion Hotel.

It is felt by the members that, although the national organizations have their definite place, they have a very close bond to the Southwest Allergy Forum. As stated above, in these meetings many a young man has been

made to feel that he has something to say—and as a result the Forum has done a yeoman service in the development of the practice of allergy. Practical topics have been emphasized and more technical presentations have generally been avoided. For all these reasons, we of the Southwest Allergy Forum feel that this organization is the queen of the sectional allergy societies.

Under the presidency of Dr. Orval Withers, a very fine meeting was held in Kansas City in 1953. During this session, it was voted to hold the 1954 meeting in New Orleans. The following is a list of the officers and Executive Committee members for the New Orleans meeting:

President—Henry D. Ogden, M.D., New Orleans.

Vice President—Vincent J. Derbes, M.D., New Orleans.

Secretary—Stanley Cohen, M.D., New Orleans.

Treasurer—Nicholas K. Edrington, M.D., New Orleans.

Executive Committee—Jack R. Anderson, M.D., New Orleans.
H. Whitney Boggs, M.D., Shreveport.
W. H. Browning, M.D., Shreveport.
B. G. Efron, M.D., New Orleans.
A. McComiskey, M.D., New Orleans.
Jack E. Strange, M.D., New Orleans.
Narcisse F. Thiberge, M.D., New Orleans.
J. Dudley Youman, Jr., M.D., Shreveport.

Because of the fact that there are two medical schools in New Orleans, it was felt that there was an abundance of good speakers who could talk on practical subjects relating to allergy. With the help of Dr. Vincent J. Derbes and other members of the Executive committee a program was arranged along these lines. This program has already been described in detail. In this Issue of the ANNALS OF ALLERGY we are presenting certain original articles and abstracts of talks that were given, which may be of interest to those who could not attend the meeting.

It should be noted that Dr. Nicholas K. Edrington gave great help to the Committee in his excellent handling of the entertainment features of the meeting. Also, Dr. Jack Anderson very capably handled the commercial exhibits. The pleasant refreshments served at the home of Dr. Stanley Cohen, where some of the organizational meetings were held, greatly facilitated the work of the committee.

HENRY D. OGDEN, M.D.

SOUTHWEST ALLERGY FORUM

FIFTEENTH ANNUAL MEETING

The Fifteenth Annual Meeting of the Southwest Allergy Forum was held May 9-11, 1954, at the Roosevelt Hotel, New Orleans, Louisiana. Sunday evening a cocktail party was given by the Executive Committee at the Court of Two Sisters. Dr. J. Harvey Black presided at the Monday morning session, and the following papers were presented: Employment of the Asthmatic In Industry, Dr. Neill K. Weaver; Primary Herpetic Gingivostomatitis, Dr. G. John Buddingh; Psychosomatic Problems in Allergy from the Spiritual Standpoint, Fr. W. D. O'Leary, S.J., M.D.; Proper Use of Trypsin Aerosol in Allergic Diseases, Dr. Albert H. Unger and Dr. Leon Unger; Contact Dermatitis, Dr. John M. Sheldon; Micro-Meteorology and Human Well-being, Mr. N. C. Roberts, Jr.

THE FIVE PRESIDENTS

(Left to right, seated): Dr. Henry D. Ogden, New Orleans, President, Southwest Allergy Forum; Dr. J. O. Weilbaecher, Jr., President, Orleans Parish Medical Society; standing, Dr. Homer E. Prince, President, American College of Allergists; Dr. Fred W. Wittich, President, International Association of Allergology; and Dr. John M. Sheldon, President, American Academy of Allergy.

There was a luncheon in the Blue Room attended by the five presidents. At the afternoon session, Dr. I. S. Kahn presided, and the following papers were presented: Selection of Molds for Therapy, Dr. Homer E. Prince; Symposium, Antibiotics in the Allergic Patient, Drs. Edwin D. Kilbourne and Alfred B. Longacre; Long Term Therapy Using Antibiotics and Chemotherapy in Asthma Associated with Infection, Drs. Charles B. Shuey and William C. Grater; Anesthesia in Allergic Patients, Dr. John Adrianni; Cortisone, the Triple-edged Sword, Dr. Albert Segaloff; Immunologic Mechanisms in Hematology, Dr. Charles C. Sprague; Classic Aspects of Onion and Garlic Dermatitis in Housewives, Dr. James Burks. On Monday evening there was a cocktail party in the Grand Ballroom of the Roosevelt Hotel, courtesy of Borden Company, followed by the Annual Banquet, which was fully attended.

SOUTHERN ALLERGY FORUM

Tuesday, May 11, the morning session was presided over by Dr. Orval R. Withers, and the following papers were presented: Pulmonary Function Testing in the Practice of Allergy, Dr. John H. Seabury; Clinical Patterns Associated with Inflammatory Disease of the Smaller Bronchi, Dr. Morton M. Ziskind; Pathology of Dyspnea, Dr. Russell L. Holman; Some Otolaryngological Procedures Useful in Treating the Allergic Patient, Dr. Jack R. Anderson; Ear, Nose and Throat Examination of the Allergic Patient, Dr. A. J. McComiskey; Cardiac Asthma, Dr. Edgar Hull. Dr. Vincent J. Derbes presided over the Luncheon in the Blue Room. Dr. James K. Feibleman was luncheon speaker. His subject was The Relation of Science to Human Culture.

Dr. Fred W. Wittich presided over the afternoon session, and the following papers were presented: Drug Allergy, Dr. Ethan Allan Brown; Amniotic Fluid Embolus. Is Death Due to an Anaphylactoid Reaction? Dr. James Henry Ferguson; Systemic Reactions Following Scratch Testing in Allergy, Dr. Ralph Bowen; Use and Abuse of Statistics in Allergy, Dr. Huldah Bancroft; A New Tuberculin Test which Determines the Amount of Allergy and Immunity to the Disease, Dr. Edward Dougherty; Eosinophilia in Childhood, Dr. John H. Dent; Preliminary Report on Results with Quinoline (Geschicter) Treatment of Bronchial Asthma, Dr. H. Whitney Boggs; The Use of Alveaire in Asthma, Sinusitis, Bronchitis and Bronchiectasis of Adults, Dr. Joseph B. Miller; The Relationship of Bacterial Infection and Respiratory Allergy, Dr. Harris Hosen; A Study in Comparison of Elimination Time Between Pollen and Molds in Man and Animal, Dr. Barney A. Credille.

There were eighteen technical exhibitors and every afternoon movies were shown on various scientific subjects.

BUTTERMILK AND ANTIBIOTICS

S. D. Manheim writes in the *New York State Journal of Medicine* 51:2759, 1951, that buttermilk has been found useful in counteracting the undesirable intestinal effects which sometimes result from antibiotic therapy. Restoration of a healthy bacterial balance is important when antibiotics or chemotherapy have an adverse effect on the normal intestinal flora. Both the simultaneous and subsequent administration of buttermilk have been of benefit even in cases with serious anorectal complications.

SODIUM CONTENT OF DIETARY FOODS MUST APPEAR ON LABEL

The Federal Food and Drug Adminstration has issued an advertising regulation effective October 1 requiring that dietary foods with low salt or low sodium content must bear labels indicating the sodium content per 100 gm of food and the amount of sodium contained in an average serving.

THE USE AND ABUSE OF STATISTICS IN ALLERGY

HULDAH BANCROFT, Ph.D.

New Orleans, Louisiana

PROGRESS in the field of allergy, as in other medical specialties, is dependent on the acceptance by the profession of the science of statistics as one of its tools. Some of you may disagree with this statement. You may say, "I do not need statistics to tell me how to successfully treat a specific patient." To answer this, let us take a look at what we mean by statistics. To some it means a mass of figures presented in tables or in a series of charts or graphs. To others it means complicated mathematical formulas applied to quantitative data. The statistician tosses around such terms as correlation, Chi-square, probability, variation, et cetera, as freely as the allergist tosses around diagnoses. In the broadest sense, however, any observation, such as the fact that the patient has a blocked nose, or any measurement, such as the percentage of eosinophils in a nasal smear, is a statistic. When numbers of such observations or measurements are made, they must be collected and analyzed if they are to have meaning. This is the phase of clinical research in which the statistician may be of great help. To the majority of practicing physicians the work of the statistician is bewildering and often foreboding. This is because the latter applies a scientific tool about which the former knows little to a problem in which he is vitally interested. This may be a difficult adjustment emotionally.

A brief study of the problem may show us (1) how the statistician may help the allergist and (2) how the allergist may help himself by an understanding of some of the simpler but important statistical concepts. As a first approach, the problem of therapy offers the broadest field for discussion. When the number of therapeutic agents available for use was limited, each physician by means of trial and error on his own patients was able to select the one agent which, for a specific diagnosis, gave the best results. Today with the multiplicity of preparations on the market the situation is different. Drug after drug has been introduced with enthusiastic reports as to its value, only to be discarded in a few months or so as worthless. Why? Because such drugs were put on the market without adequate clinical trial. A well-planned therapeutic trial of a drug in allergy has been, and still is, the exception rather than the rule. Probably some of this failure is due to the fact that animals do not develop allergic conditions as do men and hence are of little value experimentally except in toxicity studies. However, some is due to a failure on the part of the

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practicing allergist to recognize the necessity for such trials in human beings.

In what way are therapeutic trials inadequate? Probably the first and most common deficiency is that all too many drugs are tried on a small number of cases, often on as few as two or three. A first report, for example, speaks enthusiastically about the excellent results obtained. The author says, "This drug is a valuable addition for the treatment of this particular diagnosis." A second report a month or so later may even agree, but gradually conflicting reports appear. And in the end the drug may be discarded completely. Too many examples of this type of situation are to be found in the literature to justify the selection of a single one for illustration. Why do we get such conflicting reports especially when based on small samples? First, we must remember that patients vary in their response to therapy. Also, that patients vary in their response to the same therapy at different times as climatic and emotional conditions change. With a small series these varying effects may by chance all be in the direction of a favorable response. When a few more patients are added the chances are good that some of the poor responders will be included. You are all familiar with the pastime of penny tossing; if you toss two pennies repeatedly, in only twenty-five trials in one hundred will you have both pennies showing heads. In the same manner suppose you have a drug with a fifty per cent chance of producing a cure, and you treat two patients. The chance is one in four that both patients will be cured. Not until you had treated at least six patients, all of whom could be classed as cured, could you say that the event was more than you would expect by chance, and that on a basis of a fifty-fifty chance of cure in a single patient. Given a drug with a cure rate of 90 per cent, it would be necessary to treat thirty-eight patients, all of whom gave favorable results before you could state with the same degree of confidence that the occurrence was anything beyond what you would expect by chance. Such figures as these should point out the dangers of drawing conclusions on too small samples.

The second and more serious defect in therapeutic trials is the failure to use control groups in appraisal of the specific therapy under trial. That this is true in all fields of medicine is well illustrated in a report made by Ross.[10] He analyzed the first one hundred articles dealing with therapy or procedures which appeared in five of the leading medical journals between January 1 and June 1, 1950. These journals were the *Journal of the American Medical Association, American Journal of Medicine, Annals of Internal Medicine, Archives of Neurology and Psychiatry,* and the *American Journal of the Medical Sciences.* Of the reports analyzed, in 45 per cent no controls were used, in 18 per cent inadequate controls were used, in 10 per cent controls were impossible, and in 27 per cent only was the study well controlled. In articles appearing in the *Journal of Allergy* and the ANNALS OF ALLERGY much the same situation prevails. Exact appraisal

was impossible because as Kaplan[8] reports: "in most clinical papers reviewed by us, protocols were lacking." As near as could be determined by the data given, of the papers dealing with therapy appearing in these two journals for the year 1952, approximately 50 per cent reported no controls and in another 20 per cent the controls used were inadequate.

Just why are control groups necessary? In allergy there are relatively few objective measures which can be used for appraisal of results. Most evaluation must be made on subjective evidence. We must recognize, therefore, that not only do patients vary in their response, but they vary in their own appraisal of their response. What to one patient represents thirty minutes of most severe symptoms, to another may mean only minor discomfort. Controls are also necessary because the environment changes continually. Atmospheric conditions on one day may precipitate more attacks of asthma than on another day. Pollen counts vary, often radically with rapid changes in the weather. Last but not least, although we may be reluctant to admit it, patients may improve without care. Frequently diseases are self-limiting.

A good example of what happens when conclusions are drawn on uncontrolled studies can be found in the literature regarding early use of histamine azoprotein (Hapamine). Sheldon and his colleagues,[11] in 1941 reported on the results of treatment of thirty-nine patients with this drug. They stated that fair to excellent results were obtained in nineteen. In 1947, Dundy, Zohn, and Chobot[6] treated twenty patients with the same drug. They reported that the clinical results were disappointing and stated in conclusion, "We cannot subscribe to its therapeutic usefulness." In the same issue of the same journal Cohen and Friedman[2] reported on the treatment of fifty-five patients with much the same diagnosis as in the Dundy series. Cohen concluded that Hapamine was of definite value in urticaria and in certain cases of asthma. He agreed with Dundy that it was of no value in hay fever. Certainly there is disagreement between these three studies. You might argue that the differences may be due in part to the fact that in these studies the samples were not large and, therefore, there was not a sufficient number of patients having a specific diagnosis to justify drawing conclusions. There may be some truth to the statement. Much more to the point is the fact that in none of these studies were controls used.

Treatment of the common cold, a problem of interest to all allergists, provides an excellent illustration of the necessity for and the value of controlled study. It has the advantage that usually large series of cases are available and thus the criticism of small samples does not apply. Diehl,[4] in 1933, in a well-controlled study discovered that 35 per cent of patients with common colds receiving placebos of lactose alone reported good results. Self-cures then must be eliminated from the picture before any conclusion can be drawn as to the value of a specific therapy. Only by use of a parallel group not receiving treatment can this be done.

A striking illustration of the value of controls is given in early work done by Diehl, Baker and Cowan[5] on the use of cold vaccine. All persons participating in the study were volunteers and were assigned at random to one of two groups. Both groups received treatment, either an injection of the vaccine or of an "innocuous agent." The physician evaluating the results did not know to which group the individual belonged. At the end of the two-year study when results were tabulated, it was shown that the average number of colds per person per year in the group receiving the vaccine was 1.6 as compared with an average of 5.9 reported for the same group for the year prior to the study. This reduction would impress almost anyone. But an examination of the results found in the control group revealed an average of 2.1 colds during the study period as compared with an average of 5.6 for the previous period. Thus, there was a reduction of 4.3 colds per person per year in the vaccinated as against 3.5 for the control group. Completely false conclusions would have been reached had not the study been so well controlled.

Early work on the use of antihistamines in the treatment of the common cold was done by Brewster,[1] in 1947 and 1949, with a wholly unselected group and with inadequate controls. His promising results were strengthened by the enthusiasm of Gordon[7] and Murray[9] in work done in 1948 and 1949. Both of these men treated approximately 500 individuals, samples of sufficient size to give valid conclusions but unfortunately neither with any control observations. In 1950, the picture changed with the report of Cowan and Diehl[3] on a well-controlled study. They tested two antihistamines, thephorin and Pyribenzamine,® against ascorbic acid and against a placebo tablet. The results with the antihistamines were not better than those obtained with the placebo. This should emphasize again how false conclusions can be reached when control observations are neglected.

Granted then that controls are necessary, what factors should be considered in their selection? These will depend in part on the character of the problem. If you were studying mortality from tuberculosis, you certainly would need to consider age, race, and sex. If you were considering the relationship between smoking and cancer of the lung, some of the variables you would have to consider would be age, sex, whether the individual smoked cigarettes, a pipe or cigars, how many he smoked per day, how long he had been smoking, and whether he inhaled or not. The allergist is limited somewhat in his selection of controls by the fact that the number of patients with the same diagnosis available for study is relatively small. Therefore, he must of necessity in most instances ignore factors such as age, race, and sex.

There are, however, important factors he can consider. First and foremost is that the assignment of patients to treated and control groups must be made in such a manner that the groups are reasonably alike as far as diagnosis, previous treatment, and severity of disease are concerned. This

is of greater importance in small samples than the common practice of assigning alternate patients to control and treated groups, or of a random assignment to the two groups. If you could treat several hundred patients, either of the latter methods should result in groups that were fairly evenly balanced as to diagnosis and severity. However, when small numbers are involved, a form of stratification will produce groups more nearly comparable.

Second, he must make sure that every patient gets some form of treatment. To give one group a hypodermic injection at each visit and the other group nothing or even a pill will not make for valid comparisons. As far as the patient can tell it should appear that all are being treated alike—if with pills, preferably with pills that look and smell alike, even though one may contain nothing but sugar. If treatment is by injection, every patient must receive an injection; one may be of an inert substance, but it should resemble the actual drug being used. Ideally the experiment should be blind not only to the patient, as just outlined, but blind to the physician. Some may argue that it is not ethical to treat a patient with a placebo, in other words to make him think he is being treated when he is not. Is it any more unethical to treat a patient with a drug the value of which you do not know? It is particularly important if the person assessing the result of the therapy is not the same person who is carrying on the experiment, that the assessor be blind as to whether the patient has been treated with the drug or with a placebo. All physicians are human and it is almost impossible to be absolutely unbiased especially if one is convinced that the drug is of value.

In allergy, because atmospheric conditions play such a part in producing symptoms, controls and treated should be studied over the same period of time. To compare records of patients with hay fever treated with a certain drug in 1951, with a similar group treated with a new drug in 1954, is indeed false. Pollen counts vary from year to year; severity of hay fever varies from year to year even with no therapy. For this same reason the past history of a patient in regard to allergic manifestations cannot serve as a control for the present treatment.

Objective findings which can be used for assessment of results are relatively few in allergy. Patients vary in their emotional make-up as well as in their response to discomfort and pain. If placebo and treatment can be alternated in the same patient, much of this variability can be eliminated by comparing results while under treatment with those while on placebo. If such alternation is to take place, to avoid influence of atmospheric conditions it is wise to divide the group so that at all times half will be under treatment while the other half is on placebo.

The primary goal then in controlled studies is to make sure that there are at least two groups. These groups should be alike as far as it is possible to make them, except for the one variable under consideration, usually treatment. Only when such criteria are met can valid comparisons

be made. The procedures and concepts so far presented do not require any special statistical training. They do need an awareness of the factors which are important in influencing the outcome of the experiment and a determination to make sure that these factors are equalized as far as possible in the experimental and control groups.

Having made sure then that you have a right to compare two groups, the next consideration is to examine the difference between the two groups to see whether this difference is sufficiently large to have any practical significance. Here in most instances absolute differences are important. For example, suppose the cure rate with drug A is 4 per cent, as compared with a 2 per cent cure rate with placebo. Four per cent is double 2 per cent, but when you consider that 96 per cent were not cured with drug A, as compared with 98 per cent with placeboes, the difference is not so striking.

Let us assume that your groups can be validly compared and that the difference between the two groups is sufficiently large to be of practical importance. The next step is to determine whether this difference is greater than can be accounted for by chance. It is at this level that you will no doubt need to consult someone with training in statistics. This person will now take your data and using the tools of his trade in the same manner as you use your tools come up with a value which he denotes as probability (P). There are various techniques and tests which are used in calculating this value, dependent on the type of data you have. These do not need to worry you any more than you expect your patients to be concerned about how you make your diagnosis. The important thing is for you to understand what the term probability means. Probability is a measure of the frequency with which differences such as you observed would occur by chance. If this probability is very small then you can be sure that the difference you found is not due to chance but is related to the factor which differentiated your treated and control groups. The level of significance, that is the point at which you decide that chance was not responsible for the difference, will vary with different people. Most experimental studies use a level of significance based on a value of "P" equal to .05 or less. With this value of "P" if you conclude that the difference which exists is related to the factor differentiating your groups, you might be wrong five times in 100, since that is the frequency with which you would expect it to occur by chance. Obviously, the smaller the value of "P" the more sure you can be that your difference is not due to chance but is related to the variable which you are testing.

Few of you will actually set up clinical experiments, but all of you will read the results of such experiments. An awareness of some of the concepts which have been discussed in this paper should help you to better evaluate the articles you read. There is no place in clinical literature for statements such as, "The results have not been evaluated statistically but in our opinion . . ." If quantitative data are presented, they should be analyzed quantitatively. If only a series of cases are presented with

findings for each case the only conclusion that can be drawn is one applicable to this specific series of cases alone. No one is justified in projecting the results of such a series even to cases with the same diagnosis generally. Not until the application of a therapeutic agent to a well controlled series has been made can conclusions be drawn which can be applied to similar patients in general.

If you are going to carry on a research problem, until you have had considerable experience in such, you will find that the statistician can be of value to you in all stages of the problem. He can help you in the definition of your problem, in the actual set-up of the experiment including the plan for assignment of patients to groups so as to ensure that your controls are adequate. He can assist you in the form of the records you will keep so as to facilitate analysis. Finally, he can assist you in the actual analysis of your data. By consulting him early in the game, you will avoid the pitfall of ending the experiment with data that are worthless.

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Tulane University

STATISTICS

In line with Dr. Huldah Bancroft's paper, "The Use and Abuse of Statistics in Allergy," attention is called to a paper entitled "The Statistician's Place in Medical Research" by H. A. Davidson which was published in the *Journal of the Medical Society of New Jersey*, Vol. 15, page 20, 1954.

He points out the shock which many physicians receive when, having published a paper giving the effective results obtained with a new drug, other workers are not able to duplicate these results. He suggests seeking the advice of a statistician before completing the project to have all figures validated. Schools and colleges have such statisticians on their staffs, and the American Statistical Association, 1108 Sixteenth Street NW, Washington 6, D. C., will furnish a list of members in one's vicinity.

A STUDY IN COMPARISON OF ELIMINATION TIME BETWEEN MOLDS AND POLLEN IN MAN AND ANIMAL

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IT IS GENERALLY accepted that mold derivatives, such as penicillin and certain other antibiotics, are rapidly eliminated from the body tissues following oral or parenteral therapy. This poses the question: "Does a similar response follow therapeutic use of the mother molds as currently used for hyposensitization purposes in allergic manifestations, such as seasonal hay fever and seasonal bronchial asthma?" Experimental and clinical studies with mold antigen have shown that the mother molds do experience a fate identical with that which befalls certain of their derivatives.

Parallel studies with ragweed pollen extracts indicate that they do not possess similar characteristics. Among the earlier workers in the field of allergy, much interest was manifested in the rates of absorption and elimination of antigens because of the concern over the rather frequent systemic reactions from pollen therapy. Today, such reactions are rarely encountered by the experienced allergist, but the length of time antigen remains in the body tissues still is important because it does have direct bearing on the involved immunologic process. Processes of absorption and elimination have interdependent mechanisms, and any factors influencing this relationship will have a direct bearing upon the immunologic processes. An investigation of some of the fundamentals involved in the process of elimination from body tissues of fungi and pollen form the basis for this paper.

Casual inquiries of physicians interested in allergy regarding their results with specific mold therapy lead me to believe that there is some difference of opinion concerning this phase of allergy, and comments from various eminent allergists confirm the impression that mold allergy still remains a controversial subject.

Realizing that this information represented an insufficient number of physicians to be of any statistical value, questionnaire reply postcards were mailed to 870 allergists, of whom 327, or 38 per cent, responded. Replies were received from all sections of the country and thus represented a relatively accurate cross section of national opinion among physicians actively engaged in this type of therapy. Sixteen, or 5 per cent, had no experience with mold therapy. This gave 321 cards of statistical value.

An evaluation of replies revealed that 106, or 34 per cent, had unsatisfactory results in the management of their mold cases. One-hundred and ninety-nine, or 63 per cent, had better results with ragweed pollen

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extracts than with mold treatments. One hundred-eighty-four, or 59 per cent, had satisfactory results with routine mold treatments. Twenty-one, or 6 per cent, were unable to evaluate their results. Forty-seven, or 15 per cent, made a plea for standardization of mold extracts, and thirty-three, or 10 per cent, of the physicians were dissatisfied with results in etiologic diagnosis of mold sensitivity.

Numerous cards bore comments of particular interest:

"I am sure that we are, in using mold antigens, utilizing treatment material comparable to that which would be obtained by chopping and extracting a whole ragweed plant for the pollen extract." (2) stated: "I am not satisfied with the diagnosis of mold sensitivity, in most cases proving that sensitivity is still difficult." (3) "There are many false positive reactions to molds, have used all type of mold antigens and results of treatment have been uniformly poor." (4) "Feel that mold allergy is greatly overrated and I doubt that mold sensitivity is a specific entity in allergy." (5) "Greatest need is for more potent testing material as well as for treatment." (6) "I get best results with small doses of mold antigen." (7) "I treat with potent extracts and I get best results with small doses of mold antigens." (8) "Molds as a perennial cause of asthma and rhinitis are more important than pollens." (9) "I have to use high concentrations to obtain results." (10) "The best results are obtained with very low dosage maintenance rather than strong build-up doses." (11) "I discontinued using mold treatments because of uniformly poor results."

These are only a few of the many interesting comments received. Letters were received elaborating on certain points and questions that could not be included in the postcard questionnaires, and reflected the current interest in this phase of allergy. In considering the replies one is impressed with the decided differences of opinion with regard both to diagnosis and treatment of mold allergy. The fact that one out of three physicians is obtaining poor results from his treatments should arouse concern in all who are interested in this field of allergy.

Many mold extracts prepared today are potent and adequate for diagnostic and therapeutic purposes if a few salient facts are kept in mind. Although the mold season is not as sharply defined as the various pollen seasons, the history is typical, nevertheless, and a presumptive diagnosis can usually be made before resorting to testing. With potent material, the diagnosis may be confirmed in the majority of instances by scratch tests, nasal and conjunctival testing.

When 63 per cent of the physicians polled stated that they get better results with pollen than with mold therapy, some thought must be given to one physician's comment that molds are poor antigens. A group of 15 per cent advised standardization of mold extracts. Unquestionably, this is the desirable aim, not only for mold but for all antigens used in allergic therapy, and the proposal should meet only approval.

Since the early mold surveys of Durham;[3] Prince and Morrow;[10] Feinberg and Little;[5] Feinberg and co-workers;[4] Schonwald;[11] Waldbott, Ascher and Ackley;[12] Pennington;[8] Pratt;[9] MacQuiddy;[7] Wittich, and many others, progress has been steady in the development of mold extracts of superior quality both for diagnostic and therapeutic purposes.

The interest of allergists in the absorption and elimination of antigens, particularly pollen, has stimulated much worthwhile research with such antigens, but in the literature similar studies of fungi have not been found. However, worthwhile contributions have been made in the direction of determining the rate of absorption and elimination of other antigens. Cohen and co-workers[1,2] compared the absorption time in atopic and nonatopic individuals after blowing ragweed pollen in the nose and injecting the extract subcutaneously. Feinberg and Bernstein,[4] found that pollen extracts were not demonstrable in the blood forty-eight hours after subcutaneous injections. Levine and Cocoa,[6] found considerable quantities of pollen extract in the blood two days after its injection and traces remaining after seven days.

ANIMAL AND CLINICAL INVESTIGATION

The purpose of the animal experiments was to determine the relative comparison in the elimination time between mold and pollen extracts. Because of their frequent use for hyposensitization purposes, the mold alternaria and ragweed pollen were selected for this study. Extracts of alternaria were obtained from three different pharmaceutical firms for this investigation.* Three concentrated solutions of alternaria in buffered saline were designated as extracts "A", "B" and "C". A solution of concentrated ragweed extract, consisting of one-half short ragweed and one-half giant ragweed in buffered saline, was prepared in our laboratory. The lack of standardization in mold extracts and the widely varying results obtained with them were emphasized earlier in the paper. In appraising the potency of antigenic materials, reliance frequently has been placed upon the protein nitrogen content per cubic centimeter, usually converted to nitrogen units. All of the material used in this investigation was analyzed by a commercial laboratory.

Fourteen mice, each weighing 20 gm, were given subcutaneous injections of 0.5 cc of concentrated extract "A", representing 26,000 units per cc. One mouse was killed each day and the blood serum prepared was used for cutaneous testing in a purely mold-sensitive white boy aged eleven years, who earlier had given marked reactions to scratch tests with alternaria, confirmed by positive conjunctival tests. The patient's history corroborated the diagnosis. On each of the first seven days in the series of consecutive daily cutaneous tests with the serum he showed a marked

*The molds employed in the investigation were obtained from Abbott Laboratories, Arlington Chemical Co., Barry Laboratories, Inc., and Hollister-Stier Laboratories.

reaction. Moderate reactions were noted on the eighth and ninth days of the study. For the next three days mild reactions were shown and after the twelfth day no reactions were obtained.

Alternaria extract "B" representing 16,800 units per cc was used in the amounts of 0.5 cc for injections into each of a second group of fourteen mice. Again, each mouse weighed 20 gm and one mouse was sacrificed daily and the prepared serum was used in cutaneous tests of the same patient during fourteen consecutive days. Good reactions were obtained for five days, moderate reactions for three days, mild reactions for three days, and no reactions after eleven days.

Exactly the same procedure was followed under the same circumstances with alternaria extract "C", representing 6,900 units per cc and a third series of fourteen mice, each weighing 20 gm. Again marked reactions were obtained for four days and no reactions were observed after ten days.

Each mouse in a fourth series of fourteen was given subcutaneous injections of 0.5 cc of the 3 per cent ragweed extract prepared from a mixture of equal parts of short and giant ragweed, representing 25,500 units per cc. A mouse was killed at weekly intervals. A white man, aged thirty-five years, who had seasonal hayfever and seasonal bronchial asthma from ragweed, was given scratch tests at weekly intervals with the serum prepared from each of the injected animals. The patient gave a marked response to the first three tests which were one week apart, moderate reactions to the next two, a mild reaction to the sixth week test, no reaction to the seventh week test or subsequent tests.

Important differences here have been demonstrated in the elimination time of molds and pollens. A relationship between the elimination times and protein nitrogen content could not be demonstrated, but this does not preclude a relationship between elimination times and the amount of specific protein present. Controls with normal mouse serum were used in conjunction with each test. From this experiment we note a ratio of 1 to 3.5 in the elimination times between the mold and pollen antigen. One could conclude that if this same ratio is maintained in man that, clinically, there should be a difference between the therapeutic responses to the two antigens.

CLINICAL INVESTIGATION

Using a series of fifty non-allergic subjects, most of whom were nurses, reverse passive transfer studies were made with 3 per cent extracts of mold "A" alternaria and 3 per cent extract of mixed ragweed, using the serum from the alternaria-sensitive and ragweed-sensitive patients studied in previous experiment. Ten sites on the flexor surface of the upper arm of each subject were given intracutaneous injections of 0.10 cc of the concentrated alternaria "A" extract. At intervals of four hours thereafter each site was injected with specific serum containing reagen until the areas failed to react to further testing. Coincidentally, ten sites on the other arm were

injected with 0.10 cc of the 3 per cent ragweed extract and at six, twelve, and twenty-four-hour intervals each site was injected with 0.10 cc of specific serum containing reagen. In each subject a marked reaction occurred within five to fifteen minutes. In those in whom alternaria extract was injected two, or 4 per cent, showed no reactions after eight hours; eight, or 16 per cent, gave reactions for twenty hours; but no reactions were noted after twenty hours. In all subjects on whom indirect testing with ragweed was performed, reactions were given up to ninety-six hours, when testing was discontinued. Controls were used in each instance of testing. From this test there is a ratio of 1 to 6 plus in elimination time between alternaria and ragweed extract. The reverse passive transfer procedure provides a fairly accurate method of determining the elimination time of allergens, and while it may not be as accurate as the technique of cutaneous testing with prepared mouse serum, the reactions were consistent and are believed to be as reliable as reactions obtained by direct intradermal testing.

It is evident that there is a greater ratio in the elimination time of the two antigens with this procedure, apparently due to the fact that the intradermal test is much more sensitive than the scratch test.

Probably the most accurate method of determining elimination time of antigens is by parenteral administration of known quantities of material, followed by a series of intradermal injections of serum containing specific reagen. This method was used on fifty subjects with controls, eleven of whom were allergic individuals, but none of them sensitive to molds or pollens. Each of this group were given simultaneously subcutaneous injections of 1 cc of 3 per cent alternaria "A" and 1 cc of 3 per cent mixed ragweed.

A series of intracutaneous injections of 0.10 cc of specific serum reagen were given at intervals from two to twelve hours. The reactions with alternaria extract were as follows: Seventeen gave reactions up to fifteen hours, twenty-two gave reactions up to seventeen hours, and eleven gave reactions up to nineteen hours. The elimination time with alternaria averages 16 plus hours. With ragweed extract two gave reactions for thirty-two hours, seven gave reactions for thirty-six hours, twenty-three gave reactions for forty hours, and eighteen gave reactions for forty-four hours. The elimination time with the ragweed reactions averaged thirty-nine plus hours. No reactions were obtained after forty-eight hours.

One characteristic finding has been that the elimination time of molds has been much less than that of the ragweed extract. Although the ratio varies with each experiment, the ratio has never been less than two to one.

MOLD THERAPY

The evidence from experimental and clinical studies that mold antigens are rapidly eliminated from the body tissues necessitated a modification of our 1952 and 1953 pre-seasonal mold therapy program. Twenty-two clin-

ically-proved mold-sensitive patients agreed to take the revised pre-seasonal program outlined to them. Seven were patients who had previously received mold treatments and fifteen were new patients. In all patients the preliminary doses were given sufficiently early to permit attaining their maximum and maintenance doses by April first. Each patient knew that after April first he was to receive injections daily until the onset of the mold season, which in Michigan is about May first.

The majority of these patients were able to tolerate a maximum dose of 0.5 cc of concentrated mixed mold extract, and this dosage was given daily to this group throughout April. After May first, the number of injections was reduced to two a week during the remainder of the season.

With this method of intensive treatment of daily injections of maximum doses over a period of one month previous to onset of mold season, results with the twenty-two mold-sensitive patients were definitely better than results of therapy in previous years. In the past, it had been necessary with the majority of our patients to complement regular treatments with frequent intradermal injections of dilute mold extracts to confer a greater degree of relief at the peak of the season: Sixteen, or 72 per cent, of the patients in this study did not require the supplementary co-seasonal intracutaneous injections. Four, or 9 per cent, of the patients who experienced mild hayfever symptoms required symptomatic relief, but the results were good; poor results were obtained with two patients who were unable to tolerate adequate doses of mold antigen. Two, or 9 per cent, of the patients who had experienced asthma during mold season in previous years were entirely free of asthma during the season. None of the patients experienced any difficulty from accumulative effects of the frequent high dosage which might be expected with ragweed pollen antigens under a similar intensive course of treatments.

DISCUSSION

Today, much time, thought and skill have been devoted to the preparation of mold antigens for both diagnostic and therapeutic purposes. While mold extracts have not been standardized, many of them are potent and would meet all requirements of successful therapy if properly employed with recognition of the fact that they are not retained in body tissues for periods of time comparable to those observed for ragweed and other pollens. Incorporation of mold extracts in a satisfactory slow-absorbing menstrum probably would go a long way toward solving the problem, but slow-absorbing vehicles have never attained any degree of popularity in the preparation of antigens for hyposensitization purposes. Lacking this, the intensive treatment described offers a good method for satisfactory therapeutic results.

Some other contributing factors in the problem of mold allergy, which may be responsible for poor results in the management of the mold sensitive patient, are incorrect clinical diagnosis, incorrect etiologic diagnosis

of specific molds involved, improper proportion of specific mold antigens in treatment material, failure to individualize the treatment program with respect to intervals between treatments and disregarding the importance of co-existing sensitization to other allergens. An intimate knowledge of mold exposure in patient's vicinity also is very essential.

From both the experimental and clinical results presented, which demonstrate that mold antigens are rapidly eliminated, the intensive method of treatment described does offer a satisfactory method of therapy in mold allergy.

In mold therapy it would appear that more frequent treatments are indicated because of the more rapid elimination of mold antigen. It is true that the group of patients treated is too small for statistical purposes, but nevertheless an accurate evaluation was not difficult because of obvious satisfactory results.

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PULMONARY FUNCTION TESTING IN THE PRACTICE OF ALLERGY

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PULMONARY function testing in teaching and investigative centers involves a costly and time-consuming group of procedures. In addition, as attention has been directed more and more towards gaseous exchange and the diffusion of these gases across the alveolar epithelium and through the capillary walls, the methods of testing have come to require skilled technical help. Obviously, such tests can have no application in the practice of allergy.

The average practicing allergist is very busy interesting himself in adequate diagnosis and treatment. Some allergists are keenly aware of the desirability of having a method for keeping an objective record of the progress of their patients over a period of years. This is particularly true of patients with asthma and asthmatic bronchitis. The many limitations of the questionnaire and interview methods of evaluating the efficacy of therapy are well known. If pulmonary function testing can assist in diagnosis, evaluation of therapy, or recording the patient's progress, several questions are immediately posed: Are there tests available which are consistent with the demands and limitations of the practice of allergy? How much floor space does the equipment require? How much does the necessary equipment cost? How much time must be devoted to each test? All of these are questions which are asked and must be answered whenever one recommends the objective evaluation, by pulmonary function tests, of therapeutic agents for asthma.

Pulmonary function testing has very little to offer the practicing allergist by way of "gadgets" for improved diagnosis. One assumes that every allergist has fluoroscopic facilities in his office, owns a stethoscope, and is versed in the rudiments of fluoroscopy and auscultation of the chest and heart. The apparatus under present consideration provides little information which cannot be gained from intelligent fluoroscopy. However, it will do what fluoroscopy cannot do. It does provide a permanent, graphic and quantitative record.

Let us assume that when the patient with asthma or asthmatic bronchitis is seen for the first time, he will be ausculted and fluoroscoped and the findings recorded. This will demonstrate two things: how well or how poorly his diaphragms are functioning, and whether there is evident ex-

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piratory trapping. This does not demonstrate, however, how much of the difficulty represents true emphysema and how much is simple asthma. Although the fluoroscopic report may be read at a later date, there is no truly measurable or visible permanent record.

Any practicing allergist can provide himself with the means of determining four things: (1) a clinically valid estimate record of the degree of ventilatory impairment, (2) the relative amount of unrelievable expiratory trapping, (3) the difference between primarily obstructive impairment and primarily restrictive dysfunction, and (4) the breathing ability after maximum broncho-dilation on graphic record which can be compared with new records throughout years of treatment as an index of progression or control of the disease process. This will afford him an opportunity to evaluate objectively any therapeutic method on either a chronic or acute basis. Evaluation of chronic medication, as compared with a standard, is always difficult except in the perennial asthmatic.

The equipment necessary to carry out these tests is simple. A 13.5 liter Collins respirometer and a Segal-Herschfus vital capacity timed interval ruler will answer all the needs of a practicing allergist. In addition, should he want to determine the basal metabolic rate, there is no better equipment for office use. It requires no more space than any office metabolism apparatus. The cost will be approximately $750.00, and the equipment has a long life with little need for repair. If the allergist will spend two hours reading and one hour experimenting on himself with the equipment, he will be ready to incorporate pulmonary function testing into his practice. As time goes on, he may become more interested in pulmonary volumina and dynamics and want to extend the uses of the apparatus.

After learning a few sources of error in the equipment, and developing a knack of achieving complete patient co-operation, the physician will be in a position to teach an office-girl to carry out these simple procedures. Her technique should be checked periodically to make certain that she is performing the tests with the necessary interest and enthusiasm. From then on, the allergist's expenditure of time is limited to evaluating a report. He himself, however, will have to do the initial study on each new patient. Even that requirement can be circumvented if some additional money can be spent.

THE INITIAL FUNCTION STUDY

When the patient who is thought to have asthma is first studied, pulmonary function tests will not be undertaken until all diagnostic studies have been completed. Furthermore, the patient cannot be evaluated during the height of a severe asthmatic attack. However, most patients whose asthma permits them to come to the office, can carry out the necessary tests without undue discomfort.

Before testing the patient, remove the CO_2-absorbing cannister and flut-

ter valve from the spirometer. Make certain there is no water in that part of the spirometer from which the cannister was removed. Disconnect the rubber tubing leading from the mouthpiece assembly at the spirometer. Inspect to see that no water has accumulated in the dependent portions of the airways. Reconnect the tubing snugly to the spirometer outlet and inlet and open the mouthpiece assembly valve. Slowly raise the barrel of the spirometer until it is between one-half and two-thirds filled with room air. Close the mouthpiece assembly valve. See that the writing point is recording on the paper on the drum and set the kymograph speed for 160 mm per minute. The apparatus is now ready for the patient.

In office practice, it is usually more convenient to do all testing in the upright, sitting position. The rubber mouthpiece is generally used together with a nose clip. If the patient is completely edentulous, a type "A" Bennett face mask may be used and held in a snug position by the hand rather than with the head harness. After the nose clip is in place, the mouthpiece is properly positioned and the patient allowed to breathe outside air by opening the mouth assembly valve. When he has adjusted to comfortable breathing through the mouthpiece, the kymograph motor is started and the patient switched into the spirometer by closing the mouth assembly valve. After six or seven breaths have been taken normally on the rapid drum, the patient is asked to take deep breaths. After he has taken four or five deep breaths, he is switched out of the spirometer to room air and the kymograph is stopped. The nose clip is removed and the patient is allowed to breathe normally while the next part of the test is carefully explained to him.

This part of his examination is to be the timed vital capacity. The patient is told that at the end of expiration he is to take in the deepest breath possible, and then to exhale as rapidly and forcefully as he can to his maximal exhalation. Following this, he is to take in again the deepest possible breath and repeat the procedure. The examiner should be placed squarely in front of the patient and should demonstrate exactly how the patient is to perform the test. The spirometer barrel is then slowly emptied by opening the mouth assembly valve and placing a weight on the barrel. A split ring is provided for this purpose. It is used also in the detection of leaks in the apparatus. The barrel should not be pushed down rapidly by hand, as water may be forced over into the spirometer and produce respiratory obstruction. The spirometer is then refilled with room air to the same level as before, and the patient is reconnected to it exactly as he was for the first tracing. With the kymograph on fast speed, the patient is allowed to take several breaths from the spirometer. At the end of one expiration, he is then told to take in a deep, deep breath. He is encouraged in doing this. As soon as the recording pin begins to level on a plateau, he is told to breathe out. At the same time the examiner, setting an example, breathes out forcefully urging the patient to completely exhale by saying "out—out—out" as he watches the inscrip-

tion of the tracing on the drum. After expiration has reached a plateau, the patient is again told to take in a deep breath and the process is repeated. The patient is then disconnected from the machine and allowed to rest.

On the initial examination, the patient should next be given the most potent available bronchodilator or combination of bronchodilators and retested after they have had ample time to exert their effect. This will allow one to measure, and to have a graphic record of, the amount of relievable bronchospasm present. One is interested in the actual volume, in milliliters, by which the three second and total vital capacities have been increased. In the author's opinion, there are two methods at present for obtaining what can be considered maximal bronchodilation. The first and oldest method is by giving a slow intravenous injection of 0.25 gm of aminophyllin followed by the subcutaneous administration of 0.1 cc of epinephrine. The second method, which seems equally satisfactory and usually less trying to the patient, is the use of an intermittent positive pressure aerosol with the Bennett machine. One part of Isuprel® and seven parts of Alevaire® are placed in the nebulizer and the oxygen stream to the nebulizer is adjusted to give a fairly heavy mist. Ten minutes of intermittent positive pressure breathing at a mask pressure of twelve centimeters will usually produce very satisfactory bronchodilation within twenty minutes of the end of the breathing period. It is not necessary to use Alevaire, but it has proved helpful in asthmatics when used in this way. There is probably no danger associated with the proper use of the positive pressure therapy unit at twelve centimeters of pressure. Either method of bronchodilation is satisfactory, but only the latter method can be administered by an office-girl. The rapid tracing of ordinary and deep breathing is repeated followed by the timed vital capacity exactly as before.

In addition to serving as a base line for disclosing the amount of unrelievable expiratory obstruction, this determination may also serve as a base line for the comparison of other bronchodilators in the relief of acute attacks of asthma or in estimating the percentage of possible relief achieved by the chronic administration of suitable bronchodilators. After one has gained familiarity with the equipment, the initial study will require approximately ten minutes for the pre-bronchodilator study and an equal period of time after the bronchodilator has had time to exert its maximal effect. A segment of the patient's tracings on the fast drum together with either the vital capacity tracing or its calculation alone may be attached as a permanent part of the patient's office record.

The timed vital capacity is measured with the Segal-Herschfus rule from the beginning of expiration to the volume at the three second interval of the rule. The time required and the maximal volume of the total vital capacity is also recorded. This measurement requires about two minutes to perform. One can inspect the shape of the fast tracing to detect expiratory prolongation and retardation, or to find evidence of inspiratory prolongation or restriction. Additional information of the same type can be

obtained by comparing the maximal inspiratory capacity with the maximal expiratory capacity. Normally they should be nearly equal.

What does one do with this data? Aside from the matter of interpretation, one can acquire a permanent record for objective comparison of the patient's ventilatory status at intervals of months or years. If not already present, the appearance of clinically detectable emphysema can be recognized and its progression watched and combatted. The management of the patient can be altered when emphysema is more the problem than asthma. The effect of bronchial detergents and increased fluid intake with or without bronchodilators can be evaluated for the individual patient. One can show the patient clearly that certain types of therapy are advantageous. Unexpected changes in pattern or values may lead one to re-examine the patient for possible complications or the presence of other disease which may limit pulmonary function. These tracings are as valuable as a series of electrocardiograms on the patient with heart disease. Of necessity, however, they are subject to interpretation in the light of the patient's clinical status and co-operation at the time the function study was performed.

If one is to use the respirometer for the determination of the basal metabolic rate, the CO_2 absorbing cannister must be properly renewed and in place when not being used for pulmonary function testing. However, most allergists will seldom use the equipment to determine basal metabolic rate. Under these conditions, it is more convenient to leave the cannister out of the spirometer bell, to keep it sealed, and to insert it only when basal metabolic rate is to be determined. For this purpose, keep on hand a tank of oxygen.

The author believes that all practicing allergists who are interested in using this equipment should read at least two articles pertaining to graphic methods of pulmonary function testing. The first of these, "Graphic Tracings of Respiration in Study of Pulmonary Disease," by Cournand, Richard, and Darling,[1] illuminates the interpretation of the form of the tracings which are obtained on the kymograph during ordinary and deep breathing. The second article is concerned with the timed vital capacity. This article, "A Simple Method for the Determination of Vital Capacity-Time Relationships"[2] describes the use of the Segal-Herschfus rule with the Collins Respirometer.

There is evidence to indicate that the timed vital capacity, being a velocity measurement, may give much the same information as the maximum breathing capacity. Perhaps it should be noted that it may give somewhat better information about pulmonary factors concerned with breathing capacity. The effort which must be expended in a maximum breathing capacity as ordinarily determined may be considerable for the ill patient, and may also involve elements of discomfort and fear.

It is hoped that these suggestions about pulmonary function testing in the practice of allergy will prompt consideration of their use, without the

prejudice of time, complexity, or cost. The cost for equipment of such long life is certainly nominal. The complexity, for the purpose of the allergist, is such that an office-girl can readily conduct the tests if properly instructed and stimulated. Pulmonary function testing will require no more time than scratch tests, and should give at least as valuable information.

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RAYNAUD'S PHENOMENON DUE TO VIBRATING TOOLS

J. Marshall in *The Lancet,* Vol. 1, page 1151, 1954, reports that of forty workers who used vibrating tools, thirty-seven were found to be suffering from Raynaud's disease. Within three months to two years after commencing this type of work the symptoms usually developed, and were not relieved by change of jobs. Thirteen patients reported numbness, whiteness, and coldness of the fingers when the hands were warm as well as when they were chilled. Cold was not found to be an indispensable condition for development of the symptoms, although it was the most common precipitating factor.

SURVEY OF SMOKING HABITS OF MASSACHUSETTS PHYSICIANS

The *New England Journal of Medicine,* Vol. 250, page 1042, reports on a questionnaire sent to Massachusetts physicians regarding their smoking habits. Of the 4104 physicians who replied, 15 per cent stated that they had changed their smoking habits as a result of the lung-cancer publicity. More than half the doctors felt that cigarette smoking might be a cause of lung cancer, and the remainder thought it had no etiologic significance, or were undecided. Some physicians indicated that they had smoked for a number of years and did not believe that giving it up would have any appreciable effect on their health.

ANESTHESIA AND ALLERGY

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THE EFFECTS of anesthetics upon allergic patients are of interest to both anesthetists and allergists. Most problems concerning anesthesia in allergic patients are not difficult to solve. However, occasionally problems arise which tax the ingenuity of all concerned. Three classes of patients are encountered in dealing with allergy and anesthesia: (1) the truly allergic patient whose symptoms are difficult to control, (2) the known allergic patient who is easily controlled and is free from symptoms and (3) the alleged allergic patient.

In the first group are patients with hay fever, asthma or extensive cutaneous lesions caused by the allergens. Maintaining adequate pulmonary ventilation is one of the chief concerns of the anesthetist. Adequate ventilation may be difficult to maintain in asthmatics and patients with hay fever because secretions and spasms cause obstruction. Cutaneous lesions located over the site of puncture preclude the use of nerve blocks and application of masks for inhalation anesthesia may be impossible when cutaneous lesions are present over the face. Patients may be allergic to implements or drugs used for anesthesia and some are hypersensitive to the rubber and plastic materials used for construction of anesthesia apparatus.

Patients in the second, and larger group, have histories of allergy to foods, pollens, drugs and other substances. They are symptomless and are troubled only on occasions when contact is made with the foreign agent. It is seldom necessary to alter techniques or selection of drugs in these cases; it is only when a history of untoward responses to drugs exists that the possibility of allergy to anesthetic drugs must be considered.

Patients in the third group, the alleged allergic patients, are the most discussed and of the least concern. Everyone who wheezes does not have asthma and everyone who sneezes does not have hay fever. Too often when symptoms puzzle a practitioner and a diagnosis cannot be made the difficulty is ascribed to allergy. The patient considers himself allergic but has no specific information concerning the supposed handicap.

The pharmacologic effects of drugs which bear a relationship to the allergic state and its various symptoms merit discussion. The central nervous system depressants may be grouped as volatile and nonvolatile. Certain characteristics are common to the members of each group. Volatile

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drugs are inert, are not destroyed in the body, and are absorbed and eliminated through the pulmonary epithelium. The blood level is varied at will by altering the inhaled concentration which in turn alters the alveolar concentration. For this reason such drugs are called controllable anesthetics. Low concentrations yield analgesia and unconsciousness; therapeutic concentrations abolish deep reflexes. The three essential requirements of a surgical anesthetic are pain relief with abolition of reflexes, muscle relaxation and loss of consciousness. The volatile drugs meet these three requirements. They are administered by means of closed inhalers which permit rebreathing of exhaled gases and maintenance of an even depth of anesthesia.

Nonvolatile drugs differ in a number of respects from the volatile. They are administered by routes other than inhalation; the intravenous and rectal routes are used for administration of most currently available drugs; and the blood level is neither controllable nor is it an index of the total drug in the body. Nonvolatile drugs are weak analgesics and merely induce sedation or hypnosis although some induce basal narcosis, a hypnotic state accompanied by amnesia. Excessive quantities are necessary to abolish reflexes, relieve pain and obtain relaxation, because they are not analgesic. If used as the sole anesthetic agent, marked circulatory and respiratory depression result. Painful impulses pass from the periphery to the thalamus and cortex and initiate reflex activity. Volatile drugs block the passage of such impulses. These drugs must be combined with analgesic substances to abolish reflex activity. Therefore combinations of nonvolatile and volatile drugs are commonly used.

Allergy to inhalation anesthetics is uncommon. Allergy to nonvolatile drugs used for general anesthesia or drugs used as adjuncts to anesthesia is rare, but has been recorded. Most drug reactions are encountered with local anesthetics. This topic is discussed later. Experimentally, anesthetics do not prevent the appearance of anaphylactic reactions. In man anesthetic drugs, volatile or nonvolatile, may not afford protection against responses to allergens. Urticaria, bronchial spasm, hypotension and other responses to an offending agent are not necessarily obviated, even though the subject is anesthetized.

Volatile drugs are subdivided into two groups, gases and volatile liquids. Three gases are in current use, nitrous oxide, ethylene and cyclopropane. The available volatile liquids are ether, vinyl ether, chloroform, ethyl chloride and trichlorethylene. Chloroform and ethyl chloride are not used because they are cardiotoxic and hepatotoxic.

Nitrous oxide and ethylene are anesthetics of low potency. Alveolar concentrations of 75 to 80 per cent are necessary for surgical anesthesia but neither relaxes muscles sufficiently for major surgery. Both are satisfactory for superficial operations and as a preliminary to ether. Cycloproprane is much more potent. Concentrations of 15 to 20 per cent relax muscles sufficiently for major surgery. Cyclopropane has a laryn-

gospasmogenic effect and may occasionally cause bronchoconstriction. Ethylene and nitrous oxide do not. Laryngeal spasm results when high concentrations are used particularly during the induction period. Surgical anesthesia is obtained at the expense of adequate oxygenation when nitrous oxide and ethylene are used, since both gases require a high partial pressure in the alveoli for effectiveness. These gases are not used unless fortified with ether or some other drug when pulmonary insufficiency exists; otherwise there is no contraindication to their use. Adequate oxygenation is obtained with cyclopropane at all times.

The volatile liquids are effective in low concentrations (about 4 per cent) and are more irritating than the gases. The term "irritating" implies that a drug damages the pulmonary epithelium. Nothing of the sort occurs. Stimulation of vagal nerve endings causes exaggerated breathing; mucous is secreted by a direct effect on the glands. Ether and vinyl ether promote more secretions than the gases. Preanesthetic administration of parasympatholytic drugs such as atropine, scopolamine or hyoscyamine inhibit secretion of mucous. Some individuals who are not familiar with the hazards of anesthesia display their ignorance by stating they do not "believe in atropine." Anticholinergic drugs are necessary for the safe conduct of anesthesia. Asphyxia from obstruction of the airway is the most common cause of death from anesthesia; aspiration of solid, semisolid or fluid materials is largely responsible for this obstruction. Pediatricians disagree with anesthetists on the question of atropine because they fear hyperthermia. Repeated doses of atropine may cause hyperthermia but not single doses used for inhibiting secretions. If one must choose between asphyxia and hyperthermia, the latter is obviously the lesser of two evils. When anesthetizing patients with hay fever, an antihistaminic drug is helpful in augmenting the "drying effect" of the anticholinergic drug.

Ether, vinyl ether, chloroform and trichlorethylene are bronchodilators. There are no objections to the use of ethyl and vinyl ether for allergic patients. Bronchial spasm may occur during induction but disappears when anesthesia is fully established. Theoretically, Cyclopropane® should be avoided in asthmatics because of its bronchoconstrictor effect, but in most instances patients tolerate the drug without difficulties. It is often selected because induction is smooth and rapid without being complicated by anoxia. Ether may be added later.

Nonvolatile drugs currently used are tribromethanol (Avertin®), short-acting barbiturates, ultra short-acting barbiturates (thiopental, hexobarbital and Surital®), and the narcotics.

Tribromethanol is known to allergists because it has been recommended as a bronchodilator in status asthmaticus. Its use when pulmonary disfunction is present is injudicious because it markedly depresses respiration. Ultra short-acting barbiturates also depress respiration particularly in basal narcotic doses. They are never used alone, because the amount necessary to abolish reflexes also causes medullary depression. These

drugs are promptly withdrawn from the blood upon injection and stored in various tissues of the body. As the narcosis lightens, additional drug must be added to suppress reflex activity. After the procedure is completed, the accumulated drug continues to circulate about in excessive amounts, causing sustained depression of the circulatory and respiratory systems. The thiobarbiturates are spasmogenic. When administered to patients with asthma or suppurative diseases of the lung, persistent bronchospasm develops. There is no way of reversing the action because the drug remains in the body for some time. Predisposition or tendency to spasm is accentuated by all barbiturates.

Narcotics are administered as a preliminary to general anesthesia for psychic sedation. Narcotics are both analgesic and hypnotic and thus differ from barbiturates and other nonvolatile drugs. The pain threshold is elevated; pain perception is obtunded. Superficial and deep reflexes are completely abolished; sharp pain, is felt; dull pain is obtunded. Narcotics, therefore, cannot be used alone for surgical anesthesia. Narcotics are spasmogenic to visceral smooth muscle and this may precipitate bronchial spasm or enhance it, if it exists. They also diminish pulmonary ventilation by depressing respiration. Both are objectionable features in the management of asthma. Pharmacologically the opium alkaloids and their synthetic derivatives are similar qualitatively but different quantitatively. Synthetic analgesics, methadon, nisentil, and dromoran are pharmacologically similar to morphine. They too depress respiration and initiate spasm of smooth muscle. Meperidine (Demerol®) is not spasmogenic but causes respiratory depression in large doses. It is preferred to the others when a narcotic is indicated for patients with asthma.

Spinal anesthesia is ideal for surgery of the lower portion of the body. There are no objections to its use for allergic patients as the physiologic disturbances it causes involve the vascular system principally. It has been suggested that neurologic sequelae of spinal anesthesia are due to allergy. This is merely a conjecture and no scientific data exists to support this contention. Certain operations may be performed using local infiltration or nerve blocks. There are no objections to the use of block anesthesia for allergic patients unless allergy exists to the local anesthetic drug.

The muscle relaxants are an important group of drugs used as adjuncts to anesthesia. The currently-used drugs act by blocking the transmission of impulses to nerve endings to striated muscle. Curare and its alkaloid, tubocurarine, have been used extensively for a number of years but have been displaced by synthetic substitutes, such as decamethonium, flaxedil, and succinylcholine. These drugs are used for major surgery when muscle relaxation cannot easily be obtained with the anesthetic being administered. Two pharmacologic types are available: those which block the nicotinic action of acetylcholine at the neuro-myojunction and those which cause a persistent depolarization of the junctional membrane. The latter act as

though excess acetylcholine were present at the membrane. Irrespective of the mechanism involved the ultimate result is muscle relaxation. None of these substances is analgesic, hypnotic or anesthetic; however, some manifest side-effects of importance to the allergic patient. Curare, tubocurarine and its derivatives may initiate a histamine-like action which precipitates severe bronchospasm. Parasympathomimetic drugs such as eserine, neostigmine and edrophonium (Tensilon) are used to reverse the action of certain muscle relaxants, and also are capable of initiating intense bronchial spasm. It is best to avoid using muscle relaxants and their antagonists for asthmatics.

Vasopressors and hypotensive drugs are used as adjuncts to anesthesia. The vasopressors are often used to alleviate certain symptoms of allergy and therefore are not objectionable. Sympathomimetic drugs, notably epinephrine norepinephrine and desoxyephedrine cannot be used simultaneously with cyclopropane or trichlorethylene because they increase cardiac irritability and precipitate serious arrhythmias. Ganglionic blocking and sympatholytic agents such as hexamethonium, arfonad, and pendiomide are used to deliberately induce hypotension when blood loss is anticipated. As they are new drugs little data is available concerning the effects of these in allergic patients.

Administration of cortisone and related hormones should not be discontinued before operation when used in the treatment of allergic states, because adrenal insufficiency may develop during or after operation. The same or a larger dose is administered.

Untoward responses of non-allergic etiology which occur from time to time with the aforementioned drugs are easily differentiated from allergic responses. The response to drugs most misdiagnosed and confused with other reactions is intolerance. Intolerance refers to the exaggerated response caused by a therapeutic dose of a drug. Reactions due to intolerance are erroneously called allergic or are blamed upon sensitivity or idiosyncrasy. Intolerance occurs occasionally with volatile anesthetics; however, it is more common with nonvolatile drugs. This difference in drugs may be more apparent than real. Dosage of a volatile drug may be varied at will. Doses of a nonvolatile drug are fixed. Once administered they cannot be retrieved. One manifestation of intolerance is the severe depression which follows the administration of the usual amount of a barbiturate.

A response not normally the one expected from a drug indicates idiosyncrasy. Excitement, convulsions and tremors following the use of a barbiturate are manifestations of idiosyncrasy rather than allergy or intolerance.

Local anesthetics are associated with allergic phenomenon more than other types of anesthetic drugs. Yet the majority of reactions ascribed to allergy are due to intolerance, idiosyncrasy, or, most often, overdosage. After injection, a local anesthetic drug passes into the blood stream. When

the blood level exceeds a certain threshold, a train of symptoms appears which is referred to as a "reaction." Reactions are of two general types, those due to stimulation of the central nervous system and those depressing the vascular system. Excitement, tachycardia, nausea, vomiting and convulsions are manifestations of stimulation. Larger doses depress the nervous system and cause paralysis and a coma-like state. The vascular type of reaction is caused by depression of the myocardium or widespread vasodilatation or both. The cardiac output is reduced and the blood pressure falls. When vasodilatation and myocardial depression occur simultaneously, severe circulatory collapse results. The vascular and nervous systems may both be affected simultaneously. The excitement and stimulation caused by a local anesthetic drug is most effectively counteracted by barbiturates. Uninformed persons blame reactions due to overdosage upon allergy. The explanation eliminates the implication of thoughtlessness or incompetence on the part of the physician. Patients with histories of having reactions often are given the offending drug at a later date without experiencing difficulty.

Allergic manifestations of the antigen-antibody type occur after repeated exposure to local anesthetic drugs. The manifestations of such allergy are usually cutaneous. Physicians and dentists are subject to this type of reaction. Eczema of the hands, urticaria, edema of the eye lids, sneezing and other manifestations of allergy appear upon contact.

The anaphylactic type of reactions, characterized by sudden syncope after the injection of minute amounts of a local anesthetic drug, have been reported but occur so rarely that one scarcely gives them any thought in everyday practice.

Undue reliance is placed upon skin tests for determining sensitivity to a local anesthetic drug. The procedure, needless to say, is of little value. A negative response is usually obtained and gives the clinician a false sense of security. Intolerance may be detected by using the intranasal test. A baseline of pulse and blood pressure is established over a five to ten minute interval with the patient in the recumbent position. Then one drop of the solution to be used is instilled into the nostril and the blood pressure observed for the next several minutes. Two drops are then instilled, then four drops, eight, sixteen, and so on until 1 cc of the solution has been used. The blood pressure is observed at three and four minute intervals. No notable change indicates the patient is tolerant to the drug.

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THE PLACE OF SCIENCE IN HUMAN CULTURE

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THE INQUIRY into the nature of things has had a long history. Interwoven with the practical necessities, and possibly inseparable from them, there have always been attempts to interpret or discover reality. The earliest records of the cave drawings in southern France and northern Spain yield evidence which can only be interpreted in terms of this double effort. We have, in a pretty basic way, the need to stay alive both in personal terms (food gathering) and in social terms (propagation); and along with these the equally strong need to know why we are here. The results of these two needs have taken a number of forms; chief among them are: art, religion, and philosophy. The practical side of art probably began with imitative magic, the practical side of religion with the propitiation of the gods. Philosophy, as the abstract consideration of the same issues, appeared somewhat later. Indeed, it may be that philosophy had to wait many thousands of years until the classic Greeks discovered it in the seventh to the fifth centuries B.C. Thus philosophy is a tardy arrival on the scene, and as a third way of satisfying our fundamental curiosity, gives us a total of three avenues of what we may call the grand routes of inquiry.

Now it is an interesting and extraordinary fact that about the seventeenth century still a fourth route of inquiry made its appearance. This was experimental science. It began, you remember, as a matter of pure investigation. Copernicus and Galileo were not concerned with controlling phenomena or with any of the practical benefits of knowledge but only with the desire to know how things are. However, some three and a half centuries of theoretical and applied science have brought enormous improvements into every corner of human activity. The theoretical benefits of science have been to add to the sum of human knowledge and to satisfy somewhat the passion for knowledge. That science has even aided the other grand routes of inquiry is obvious. Consider, for instance, that as a result of scientific technologies, we have new arts (the cinema) and new aids to art (the engineering advances in contemporary architecture). Consider, also, the aid that science has given religion. Medical science has saved many lives, reduced pain and extended longevity; and has learned from other sciences new aids to health; for instance, from physics (roentgenology) and from chemistry (pharmaceuticals). It is therefore true that religious persons as a result of the benefits of science have twice as long in which to pray.

Several questions concerning the fourth grand route of inquiry which

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is science immediately arise. The first question concerns the number of routes: where there have been three and now suddenly there are four, could not there be five or six or even more? If, in other words, after a very long period in which men lived entirely by art and religion, they suddenly acquired philosophy, and then after another long lapse acquired science, what reason is there to believe there could not be a fifth grand route of inquiry, and a sixth, and others still, the nature of which we cannot now envisage?

The second question concerns the fate in various cultures met by the institution of science as it spreads to other cultures from the one in which it was discovered. We shall not here primarily be concerned with the first question but only with the second.

Let us bear in mind for the moment, then, the very important distinction between theoretical and applied science. That theoretical science does not need applied science in order to progress is evident from the history of science. The whole scientific enterprise began with theoretical speculations and theoretical inquiry and with experiments conducted to test these—and not with any practical aim. Applied science, however, does need theoretical science in order to progress, for, as the very term itself indicates, applied science is theoretical science applied. Phrased differently, it is theoretical science that applied science is applying. Thus we see that in order for practical benefits to continue to flow from the institution of science, theoretical as well as applied science must be preserved. Moreover, theoretical science must run on ahead, so to speak; it is an undertaking which should be amortized as society's investment in the welfare of its own future.

Science as a grand route of inquiry began in the seventeenth century with theoretical science, but this fact must not blind us to the interaction which takes place between theory and practice. Theoretical science led to applied science, but the reverse reaction has also happened frequently. Developments in applied science have often led to improvements in theory. No doubt theoretical biology has been greatly stimulated from time to time by the significant data uncovered by medical practitioners. Our knowledge of the laws of aerodynamics would not be what it is were it not for our interest in improving the design of airplanes, and the same interest accounts for our new knowledge of the fast air currents which form a regular pattern in the stratosphere. Theoretical and applied science now interact greatly to the benefit of both types of inquiry and research. But while theoretical and applied science aid each other and thus have a common aim, they do also retain their separate aims. The aim of theoretical science is to increase our knowledge of the laws of nature; the aim of applied science is to utilize this knowledge for practical human benefits. And the crucial point to be made is that both aims will suffer if they are confused. Only the things which have been properly distinguished may be properly related, and science as a whole will suffer greatly if those

practical benefits we derive from theoretical science are allowed to be put before it and so interfere with its progress on its own level. To hold theoretical science down to the practical level is truly to kill the goose that has been laying the golden eggs.

We now come to our main topic, and this is the prospects of the fate of science in the hands of differing cultures in our time and for the immediate future. Science, as we have noted, began in western Europe in the seventeenth century and was there cultivated first. It has since spread to many countries; among these are: the United States, the Soviet Union and China. Every culture in which science is taken seriously understands it somewhat differently and so takes it in another direction. It is difficult if not impossible for those trained in social anthropology not to see that no institution is regarded from the same point of view in the hands of different peoples. Like the more basic institution of the family, the institution of scientific inquiry may have an altogether changed emphasis from one culture to another. We shall consider chiefly two instances: the United States and the Soviet Union.

In the United States, for instance, theoretical science may be respected, but it is primarily applied science which is pursued. Faraday discovered the dynamo in his wife's kitchen. When he presented the information to the Royal Society he was asked of what use it was, and he is said to have replied, "Of what use is a new born baby?" Neither he nor any one in his time could have foreseen the enormous size and number of dynamos produced nowadays by a single manufacturing company, by the General Electric Company, for instance. The success with which we have extended the benefits of applied science to millions of people is something which is both astonishing and wonderful. The humblest American lives better, in a material way, than does his opposite number in any other country—better than he ever has—and all a result of the spread of applied science. Theoretical science, however, has not fared so well. Until recently, it was not possible to show any theoretical advances in the continental United States which have been made by Americans, advances comparable, say, to the discoveries of Newton and Freud, or to those of Einstein and Planck. We have depended upon Europe for theories while we have counted on ourselves to discover and utilize practices. Now, of course, there is no reason to take a nationalistic view of this division, or to be chauvinistic about science. Science is by its very nature transcultural. For what we know about the regularities of the behavior of phenomena do not, except in social matters, confine themselves to any one culture but must be true throughout the world. Thus, if we could count upon Europe to continue to produce theoretical science in the future as it has in the past it would mean that, together with our splendid abilities at application, there would be no reason in particular to feel the need to cultivate theoretical science here. But is this an acceptable picture of the state of affairs? Given the condition of Europe today, it is very likely that the wars of depletion and

the economic changes may prevent or retard the kind of theoretical development in science in the future that has been produced there in the past. So it may devolve upon us to supply the deficiency in order that science may survive. If Europe is to falter, then we must produce theoretical as well as applied science—if only for practical purposes.

Now let us turn to science in the Soviet Union. If the reports we have been receiving are true, then the whole of the scientific endeavor in communist Russia is devoted to applied science and technology. And there are reasons for believing that these reports are true inasmuch as dialectical materialism—the philosophy of Marx and Engels—rests on a naively understood and now very much out-dated conception of a stubborn and irreducible matter, and so requires the elevation of applied science and the derogation of theoretical science. Theoretical science the Russians mistakenly believe to be idealistic and a product of the capitalist system. Now the first charge is untrue in the sense in which they mean it and the second is irrelevant. A good enterprise, like any other good, is good whatever we call it and whoever produces it. The need to inquire how things are must be just as relevant to the proletariat as it is to the capitalist, for curiosity is no respecter of persons. The attempt to interpret every social enterprise on the basis of economic class evaluation overlooks the universality of the fundamental human drives, and the desire to know is just as fundamental as the desire to feed and breed. If what I have said about science in the Soviet Union is true, then the only hope for the future of science lies with the Americans, since they are the only ones at present who are able and likely to develop theoretical science.

There are, of course, on the horizon dangers which may threaten the development of theoretical science here. Let me name three.

Chief among these, I suppose, is the time that often elapses between new developments in theoretical science and the discovery of how these can be utilized in practice. A good example was the length of time between Faraday's discovery of the dynamo and the lighting of our cities. An even more fantastic lapse of time took place between the discovery of conic sections by Apollonius of Perga in the third century B.C. and their applications about eighteen hundred years later! Very often men with a practical turn of mind who fail to understand this delay grow impatient with theoretical science before its applications have been discovered, for it seems to them to be a thoroughly useless pursuit. Their tolerance is somewhat short if they cannot be convinced that future practicality requires the pursuit of "useless" knowledge and therefore they may bring this pursuit to an end.

A second danger lies in the fact that technical knowledge in the sciences has outrun popular understanding. The time was—and we can pick for this purpose any period before the seventeenth century—when the masses knew pretty well everything that was going on in their day. There were no technical secrets of which they might suddenly become either the bene-

ficiary or the victim, as, for instance, our masses do from the advances in medicine or the development of atomic weapons. But since the highly technical developments of mathematical and empirical science, we are no longer able to furnish information as fast as it is increased; and ignorance concerning the true meaning of science as well as the details of the swift developments occurring in the various sciences continues to be a general condition for the layman. The public relations of the scientific enterprise are, one might say, in a frightful way. Now, nothing can continue for very long in human society that does not receive at least tacit mass support, and this can be withdrawn at any time. Men may very well grow suddenly weary of being pushed in this direction and that by forces issuing from the laboratory in some (to them, at least) mysterious fashion; and when they have had enough, they will bring it to an end. The "revolt of the masses" is always a possibility, and this again could be the death of science.

The third danger lies in the slow development of the social sciences. Thus far the social sciences have not developed as rapidly as, say, the physical, the chemical, and the biological sciences. This is not because the social scientists are any less capable or intelligent, but merely because they have attacked more difficult problems. If we consider men to be a natural product, then arguing from the relations between the sciences it is possible to assert that the higher fields investigated by the sciences consist in complications of the lower ones. A cell is more complicated than a molecule, just as a molecule is more complicated than an atom. But similarly, an organism is more complicated than a cell and an organization of organisms (a society) is more complicated than an organism. That social science is a possibility seems likely, but its development will take a long time because it will require the protracted efforts of many trained investigators. In the meanwhile, of course, what is happening in society is full of dangers for science. Wars could conceivably bring to an end the whole of scientific inquiry. The problem, then, for social science is simply this: will society leave social science alone long enough for social science to produce a science of society which can be applied to society and so perhaps save it?

Civilization is young. Individual lives are brief and while human cultures last longer, yet measured against cosmic changes they, too, seem short enough. After many thousands of years of stagnation, of trial and error successes, mankind seems to have stumbled upon a reliable method for advancing the sum of knowledge and with it of improving the human condition. The fourth and last of the grand routes of inquiry, which is science, holds great promise; for we have only to note what it has accomplished in a mere three centuries. What it could do given a respectable run of time, given, say, anything like the thousands of years which have been allotted to the arts and the religions, is difficult to picture; before its possibilities the faculty of the imagination stands amazed.

If science is to be left free to develop its enormous potentialities, we

must remember that while the truth is in no one's exclusive custody, science as a working enterprise is an human institution and as such one among a number of the institutions which make up the sum of human culture. It must be cherished by the others and its speculative as well as practical sides allowed to proliferate; and it must be protected for that purpose, for it remains one of man's last hopes.

Tulane University

HOOVER NAMES DOCTOR KLUMPP MEDICAL TASK FORCE CHAIRMAN

Former President Herbert Hoover has appointed Theodore G. Klumpp, M.D., president of Winthrop-Stearns, Inc., pharmaceutical manufacturer, as chairman of the Task Force on Medical Services of the Hoover Commission on Organization of the Executive Branch of the Government to succeed the late Chauncey McCormick of Chicago.

Objectives of the Task Force are to provide better medical care for beneficiaries of the Federal medical program; to create a better foundation for training and medical service in Federal agencies; to reduce the drain of doctors away from private practice; to provide better organization for medical research; and to provide a better state of medical preparedness in event of war. The overall purpose of the investigation is to promote economy and efficiency in the executive department.

Doctor Klumpp was chief of the Drug Division, U. S. Food and Drug Administration, from 1936 to 1941. Just prior to becoming president of Winthrop-Stearns, Inc., he was director of Drugs, Food and Physical Therapy, and secretary of the Council on Pharmacy and Chemistry of the American Medical Association. In 1951, he was chairman of the Office of Defense Mobilization's Task Force on the Handicapped. He is president of the National Pharmaceutical Council, a vice president of the American Drug Manufacturers' Association, a past president of the American Pharmaceutical Manufacturers' Association, a director of the World Medical Association, and a member of the Advisory Committee of the New York State Legislative Committee on Problems of the Aging.

Doctor Klumpp has been a member of the Task Force since its inception.

PSYCHOSOMATIC SYMPTOMS FROM A SPIRITUAL VIEWPOINT

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PERHAPS it would be better to say "those symptoms with a religious basis," for the reason that we may be better able to detect the religious factor, whereas "spiritual" may be too vague. This paper hopes to limit the subject thus: "Religion in the person as a source, or factor, in allergies," and the religious aspect will be used largely as an influence in the personality. Hence, we are not treating religion in the abstract but a person affected in varying degrees by religion. We notice, for instance, differences in emotional reactions in Catholics of various nationalities as English, French, Italian or German. Naturally, the emotional element will be of prime interest to us here.

In general, we may say that religious people tend to fall in the classification often used of "perfectionist." Such a person expects a great deal of himself, of others, and of the world. Some time ago, in dealing with adolescents, it seemed to me that we could express this idea symbolically in a formula like this, "X — Y = Z." In this formula X represents the dream self, the hoped-for self, or the desired self; Y represents the self as the person sees it; and Z represents the reaction to the difference. In this formula, the very important thing is not the absolute value of either X or Y but the relative values, thus making the minus sign significant. Another point to be stressed is the subjective value of Y; that is, not the person as he is but the person as he sees himself with relation to the person he hopes to be.

People who are perfectionists are usually idealists and do not like to be "average," or rather we should say that *their* average is very high. Some years ago, in the early days of Pullman cars, an old Jesuit priest took his first ride on the Pullman, and on getting off he said to the porter, "I understand that it is customary to give some gratuity to the porter, so tell me what is usually given." The porter said, "Well my average is $1.00." At this time the dollar had not suffered the humiliating effects of inflation and one dollar seemed quite a lot. The old priest said as much, but added that he wanted to do what was right, so he gave the porter a dollar and immediately got this startling reply. "Thank you, boss; you are the first man who has ever come up to my average since I have been on this road." He had an average but no one came up to it; in other words, he had a mental goal or expectation which had not been reached. So it is with most of us, and the situation is more acute with perfectionists.

Another characteristic of this group is the tendency to be hypercritical of themselves or to overstress their failings. This emphasis of the negative

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might be illustrated by a story told of a very wealthy little boy between five and six who was found crying by his mother. When asked what was the trouble, he said that he wanted to be like little Willie down the street. His mother was surprised and pointed out that the boy had nothing, no parents, no playthings. The disconsolate little fellow replied, "I know, but he can wiggle his ears." The fact that the wealthy boy was unable to accomplish this feat caused him to be most unhappy. Several years ago, there was a popular song entitled "Accentuate the Positive, Eliminate the Negative," but perfectionists do just the opposite.

A person who is idealistic and has religion added to his drives may find the above-mentioned equation further unbalanced, because he thinks God expects a great deal of him, and he is able to do so little toward reaching these expectations. We may express this in a further extension of the formula thus:

$$(X - Y)\ (X' - Y') = Z$$

Here X′ represents what God expects of him. Y′ represents what God sees in him (both concepts, of course, are in the patient's mind). Again Z is the reaction. However, as will be seen, the reaction is intensified because in both cases the things expected of him have been exalted, while at the same time the opinion he has of himself is lowered. This brings about a guilt feeling, although the patient has done nothing sinful. He feels guilty because he has failed himself and Almighty God. He expects much, God expects much; he sees very little, God sees very little.

Now, the Z in the formula or the reaction quite often takes a psychosomatic form in the external expression. The general dissatisfaction with self is manifest by such symptoms as sweating of palms, skin eruptions, especially on face and hands, palpitation, various forms of fears, diarrheas, et cetera. For example, if we find a young lady of thirty or thirty-four (unmarried) who has an unaccountable allergy or migraine attack, it might be well to look into her marital prospects. She may be battling with many frustrations such as fear of marriage, yet a great desire to marry, possessive parents, a non-Catholic boy friend; and her religious ideas add to her natural frustrations. She has a commandment to love and obey her parents, yet in this case where the parents oppose her, she does not love them and does not want to obey; or she may have wrong ideas of marriage and is resentful of the fact that her parents did not instruct her properly.

All this information has to be obtained slowly without breaking down the patient's defensive mechanism, avoiding scolding or sarcasm. Care must be taken not to upset the religious ideas of the patient, but to show how anxieties can be increased in a very sensitive person. As a rule, these people are sensitive, have their feelings easily hurt, are quickly disappointed in themselves and others, are hurt by injustices, and are easily discouraged. They want to be liked, but are afraid of risking themselves in a situation where they might not be liked.

These patients must be shown that it is necessary to like themselves first, and then they can like others who will like them in return. Three steps may be pointed out to them, first, tolerance of oneself; second, acceptance of oneself; and third, liking oneself. Religious people may confuse this with pride and say that pride is sinful and hence must be avoided, but it can be demonstrated that real humility is a positive virtue and not the negation of pride. Also, it takes a tremendous amount of humility to accept oneself, especially with all the imperfections so intolerable to the perfectionist. These people are continually telling themselves that they are "no good," and yet they *feel* that they are clever, talented. This is not an inferiority complex, for often it is a superiority complex. They are aloof from the crowd. They are timid and retiring, afraid to try something for fear that it will not be perfect. There is a saying, "The best is the enemy to good," and it is true here, for while waiting for the best, much good is lost.

There is a beautiful story in the Gospel about a very small man named Zaccheus who heard that Jesus of Nazareth was coming down the road, and he was very anxious to see the famous prophet. The crowd was so great and he was so small that he was unable to see. So he did a very simple thing, he climbed a sycamore tree, and our Lord rewarded him, for He said to him, "This day I shall eat in thy house." Now it seems to me we can draw a fine psychiatric moral from this. Zaccheus could have become very paranoid and raved about the crowd pushing him aside because of his size, or he could have blamed his parents for being small and thus giving him a short stature, or he could have said he didn't want to see Christ anyway. However, he overcame his disadvantages in a very practical and workable manner, and he was rewarded. Now, most of us fall short of our expectations, but there are a great many psychological trees nearby for us to climb and thus overcome our shortcomings.

With religious people we can use religion to help them as part of the treatment. They have a commandment to "love thy neighbor as thyself," but if they do not love themselves, how can they love the neighbor? Or to put it another way, if they are logical, they could do all kinds of hurtful things to the neighbor, for that would be the way they want to treat themselves. Treatment of allergies is like treatment of any other disease in that we must treat the *whole* person and not merely the disease. The emotional life of the patient is very important in allergies and it has to be taken into consideration. How he feels about himself and his religion is a very prominent part of the whole person. Such a person is likely to take himself very seriously, and often lacks a good sense of humor. If we can show him that real humility requires a good sense of humor, we shall do much. In other words, the ability to laugh at oneself requires the greatest type of humility.

We can also show such a patient that too much attention to himself will cause emotional upsets, and by forgetting himself he will become more efficient and peaceful. Here, again, we can use religion as therapy, for our

Lord said, "He who loses his life for my sake shall save it." So we get the attention diverted from the person himself to the work he has to do for the world and for God. It is a sad thing to see how difficult it is for good people to use the talents given them by God, while the wicked in the world have no trouble using their talents for evil.

SUMMARY

From this, we can see that certain manifestations of allergy may be brought about in part by hypercritical attitudes in patients who fall in the class of perfectionists. Further, religious feelings may intensify one's dissatisfaction with self and thereby intensify the allergy. Finally, religious ideas properly handled can be used for therapeutic purposes to great advantage.

Loyola University

GEIGY INTRODUCES STEROSAN® FOR SKIN DISORDERS

Geigy Pharmaceuticals, division of Geigy Chemical Corporation, has introduced to the medical profession a new prescription specialty for the local treatment of skin disorders. Sterosan® is an iodine-free oxyquinoline derivative, not related to the antibiotics, sulfas or hormones. It is available in two forms, cream and ointment, the cream being indicated for moist lesions while the ointment may be applied for conditions with a minimum of exudate. Both forms contain 3 per cent chlorquinaldol (5,7-dichloro-8-hydroxyquinaldine) as an active constituent.

Sterosan has been demonstrated to be an effective bacteriostatic and fungistatic agent against a wide range of skin pathogens, including those involved in dermatophytosis, folliculitis, impetigo, sycosis, and other infectious dermatitides. The preparation is well tolerated over large body surfaces for long periods with minimal irritation, it acts in the presence of purulent discharges which frequently block the action of topical agents, and it is stable, non-bleaching and practically non-staining.

CORTISONE, THE TRIPLE-EDGED SWORD

ALBERT SEGALOFF, M.D.
New Orleans, Louisiana

WE HAVE always been accustomed to thinking of therapeutic agents as double-edged swords, i.e., having good as well as bad effects. However, with the introduction of cortisone, and also incidentally, ACTH (but not as well proved), it has been necessary to think of this therapeutic agent as a triple-edged sword, as it has in addition to the salutary effects desired of medication and the usual commoner type of immediate deleterious effect, a third edge to its sword, a series of delayed deleterious effects, which, if not recognized and compensated for, may actually result in death of the patient. These delayed effects may not be apparent for months or even years after cessation of use of the drug.[1]

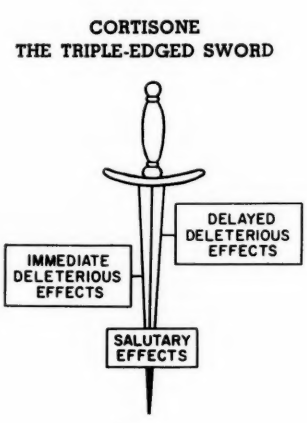


Fig. 1.

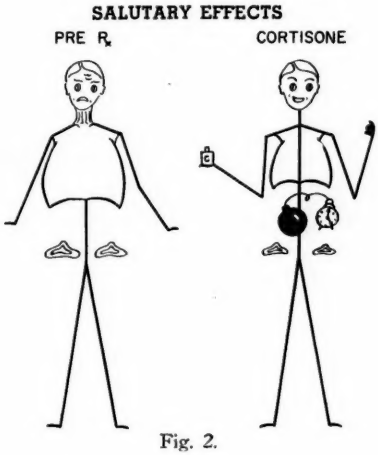


Fig. 2.

Figure 1 illustrates this concept. The salutary effects of cortisone are much too well known to discuss in detail here. Figure 2 illustrates a patient with severe asthma before and after treatment with cortisone. However, as will be brought out in the remainder of this discussion, he has also acquired something else, i.e., the "time bomb" of the delayed deleterious effects. Figure 3 likewise shows the salutary effects of cortisone in a patient with rheumatoid arthritis, who experienced a remission but has also acquired the time bomb.

From the Department of Medicine, Tulane University School of Medicine, and the Endocrine Research Laboratory of the Alton Ochsner Medical Foundation.

Presented at the Fifteenth Annual Meeting of the Southwest Allergy Forum, New Orleans, Louisiana, May 10, 1954.

Figure 4 shows the difference in the salutary effects with ACTH. Although there is still no positive proof that delayed deleterious effects follow administration of ACTH, these patients should at least be considered

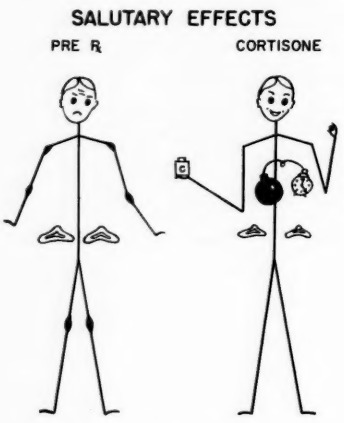


Fig. 3.

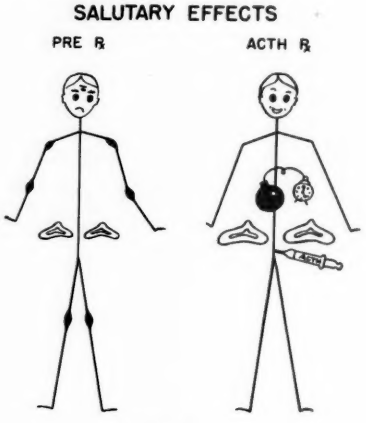


Fig. 4.

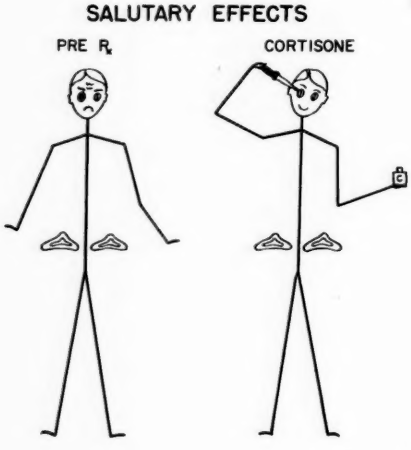


Fig. 5.

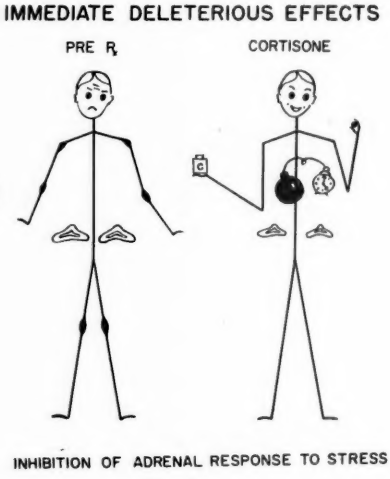


Fig. 6.

as potentially harboring them. The difference here is that instead of adrenal atrophy, as occurs in patients with cortisone therapy, adrenal hypertrophy results from the stimulus of ACTH, and there also is relief from the rheumatoid arthritis.

Figure 5 illustrates one of the salutary effects of administration of cortisone without concomitant delayed deleterious effects. The drug is

given as drops in various diseases of the eye. In general, in the amounts employed for local application, cortisone probably does not produce adrenal atrophy, so that the delayed deleterious effects in the usual dosage would not occur.

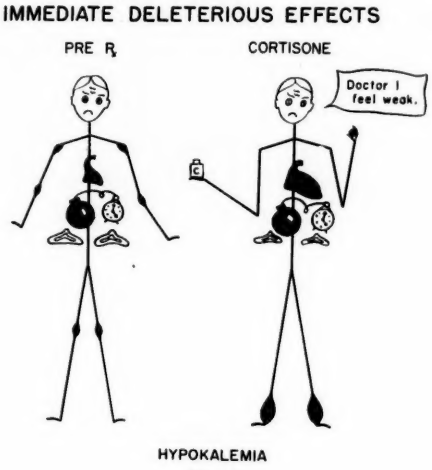


Fig. 7.

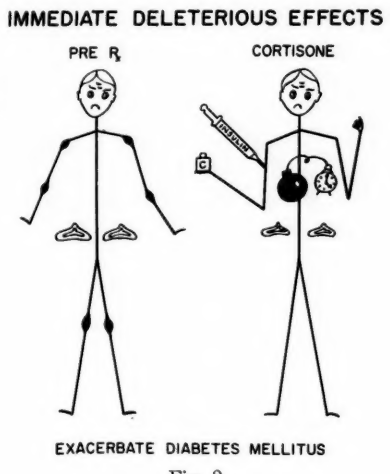


Fig. 8.

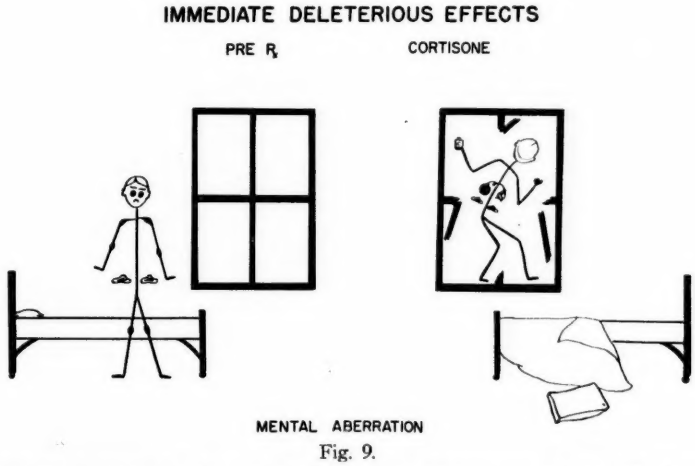


Fig. 9.

Figure 6 shows the first of the immediate deleterious effects. Cortisone, in therapeutic dosage, inhibits production of ACTH by the pituitary and results in adrenal atrophy, which in turn, inhibits the normal response to stress. This is the first and a major deleterious effect of the administration of cortisone.

The next immediate deleterious effect (Fig. 7), hypokalemia, is due to

the fact that the major effect of cortisone, ACTH, and many of their related corticosteroids, on mineral metabolism is loss of potassium through the urine, producing a state of hypokalemia with hypokalemic heart failure

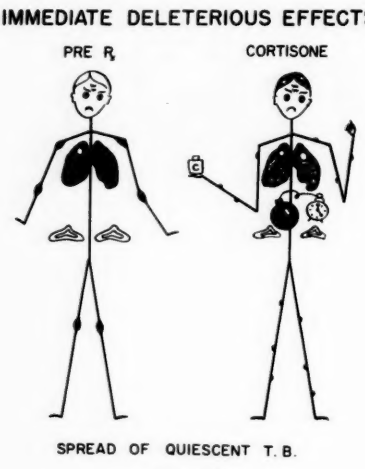


Fig. 10.

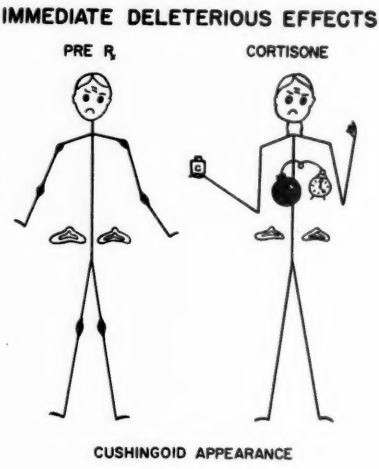


Fig. 11.

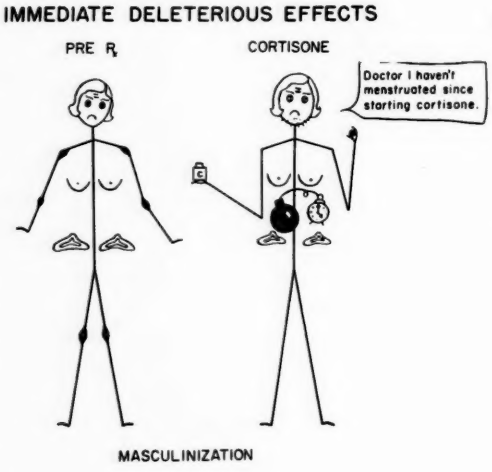


Fig. 12.

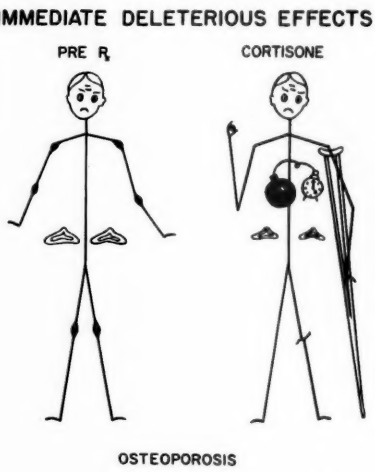


Fig. 13.

with an enlarged heart, electrocardiographic changes, and dependent edema, together with the usual overwhelming feeling of weakness.

Following administration of cortisone to patients with diabetes mellitus (Fig. 8) the disease becomes worse necessitating increased amounts of insulin.

Another serious deleterious effect is illustrated in Figure 9. Development of emotional disturbances is not uncommon following administration of cortisone and some patients have even committed suicide.

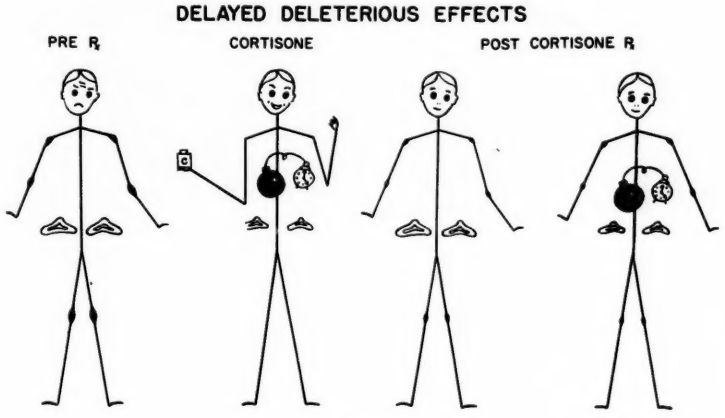


Fig. 14.

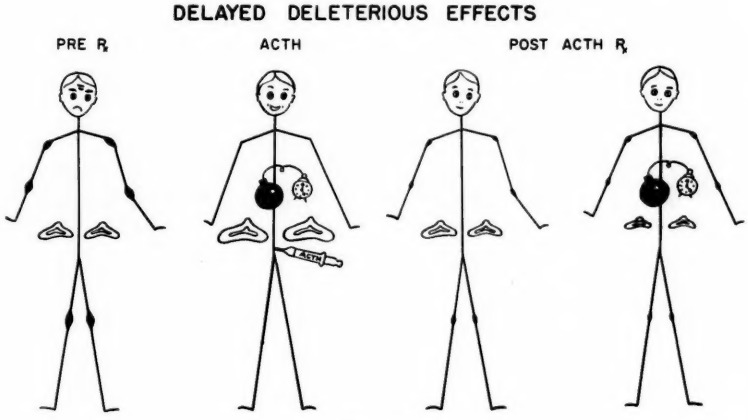


Fig. 15.

Therapeutic doses of cortisone decrease the fibrous tissue and break down the fibrous capsule around many old acid-fast lesions and can produce, as a complication, the military spread of a previously quiescent acid-fast lesion (Fig. 10).

A Cushingoid appearance develops in many patients soon after administration of cortisone (Fig. 11). Another untoward reaction which sometimes occurs is masculinization, not only manifested by facial hirsutism but also induction of amenorrhea (Fig. 12). Prolonged large doses of

cortisone produce true osteoporosis, which may lead to fractures (Fig. 13).

The delayed deleterious effects (Fig. 14) are manifested in those patients who fail to respond to withdrawal of cortisone or (Fig. 15) ACTH

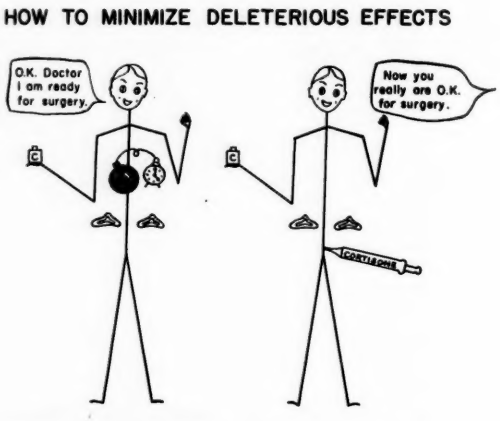


Fig. 16.

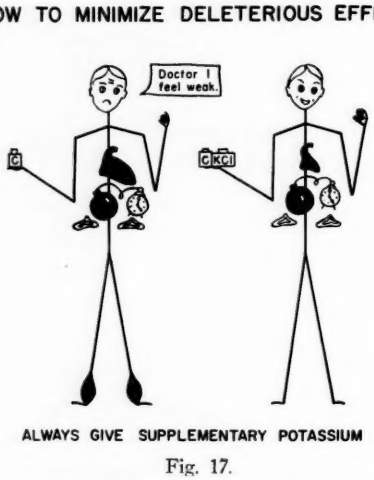


Fig. 17.

therapy with the return to normal of the pituitary adrenal axis. These patients have late-retained atrophy of the adrenal cortices, or in the case of ACTH the atrophy develops late after withdrawal of therapy, and although an atrophic adrenal gland may produce sufficient cortical hormone for all ordinary needs, it is incapable of responding in a normal manner to stress, either trauma, illness, or surgery; and these patients must be given supportive therapy.

What can be done about deleterious effects, or how can they be minimized? If a patient is expected to undergo a period of stress as shown in the next figure (Fig. 16) he should be given supplemental cortisone

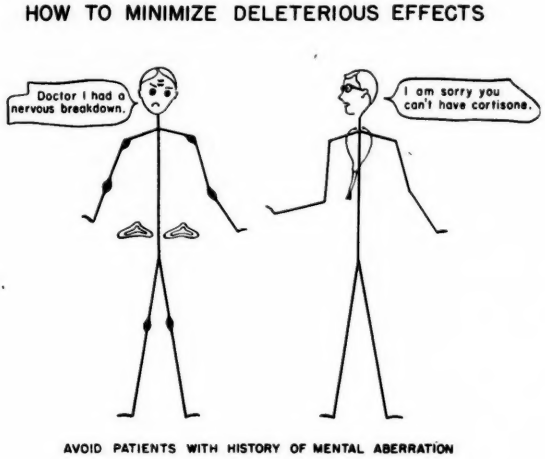

HOW TO MINIMIZE DELETERIOUS EFFECTS
Doctor I had a nervous breakdown.
I am sorry you can't have cortisone.
AVOID PATIENTS WITH HISTORY OF MENTAL ABERRATION

Fig. 18.

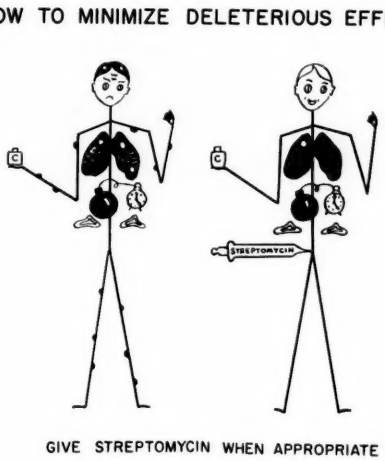


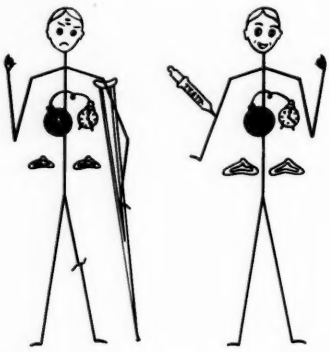
Fig. 19.

parenterally prior to the anticipated stress.[3] If the patient sustains an injury or becomes gravely ill, the additional cortical hormone should be given parenterally with Compound F or adrenal cortical extract intravenously.

Hypokalemia is a preventable complication. It is my conviction that

potassium should always be given to every patient receiving therapeutic doses of either cortisone or ACTH (Fig. 17). This is usually given as potassium chloride in daily doses of three to four grams.

HOW TO MINIMIZE DELETERIOUS EFFECTS



TESTOSTERONE PREVENTS OSTEOPOROSIS

Fig. 20.

It is impossible to predict which patients will respond to therapeutic doses of cortisone and ACTH with mental aberration. Some evidence suggests that the larger the dosage the greater the incidence of this complication. It does seem wise to avoid when possible, administration of cortisone or ACTH to patients with a history of mental illness (Fig. 18).[2]

Patients with proved quiescent acid-fast lesions should be given antibiotics when it is necessary to give them either cortisone or ACTH (Fig. 19).

The concomitant administration of testosterone and cortisone should prevent the development of osteoporosis (Fig. 20).

As discussed previously, because of the nature of the problem of cortisone and ACTH complications, it would seem wise to give therapy in short courses using minimal effective doses, and if cortisone is the drug to be used, it would probably be wise to give ACTH before stopping cortisone therapy (Fig. 21).

It is desirable for all patients, while receiving cortisone and ACTH, to carry a card (Fig. 22), indicating how much they are taking. It would also be helpful if they carried these cards for at least one year after therapy has been discontinued.

Investigators at the Mayo Clinic have set forth a series of criteria for the use of supportive therapy in patients who have had cortisone or ACTH in the past. It is their belief,[3] which I share most heartily, that it should be assumed that patients who have had sufficient cortical hormone therapy

to produce signs and symptoms of hypercorticism have atrophic adrenals for at least one year after cessation of therapy. They also presume that anyone who has received cortical hormone in significant amounts within

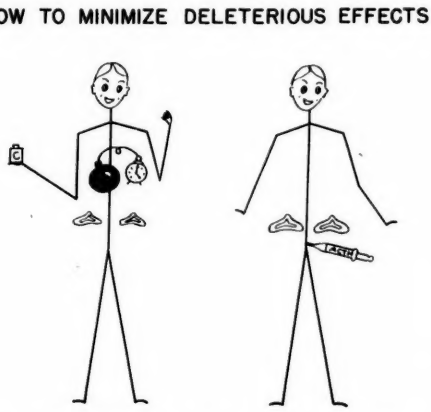


Fig. 21.

Fig. 22.

three to six months should receive prophylactic treatment for stress. If therapy has been prolonged and severe symptoms of hypercorticism have been produced for a prolonged period of time, then probably, one must assume that atrophic adrenals are present for even a longer period of time.[4]

If one knows only that a patient has had cortical hormone therapy, it is wiser to treat him for stress as though he had received sufficient cortical hormone to produce hypercorticism.

It is my opinion that if there is any doubt as to whether cortical hormone support will be necessary during operation, it is better to give it. I have encountered no difficulty from following such a rule.

I prescribe 200 mg of cortisone acetate parenterally daily, starting, if possible, forty-eight hours preoperatively, repeating this dose twenty-four and two hours before surgery, and continuing until the second postoperative day; and then gradually reducing the dose so that on the sixth or seventh postoperative day, cortical hormone therapy is completely withdrawn. It should be remembered that if the patient is being carried through surgery, he will often be unable to eat; for this reason the intramuscular cortisone should be administered earlier so that it will be absorbed during the period in which the patient is unable to take oral medication. This should be continued as parenteral therapy until the patient is on a full oral diet.

This presentation is not intended to make physicians fearful of prescribing either ACTH or cortisone when indicated. All physicians prescribe drugs every day which have untoward reactions, but it is with the knowledge that the salutary results more than justify the risk of the deleterious effects. The same should, of course, be true of cortical hormone therapy. However, the very nature of the illness so frequently treated with cortisone, ACTH, or both, is such that prolonged massive doses are often necessary. It has been my intention to alert the physician to the complications of cortisone therapy, so that he can try to prevent the preventable ones and recognize the others when they occur.

ACKNOWLEDGMENT

The assistance of Miss Dorothy Butler in preparing the illustrations is gratefully acknowledged.

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THE ASTHMATIC IN INDUSTRY

NEILL K. WEAVER, M.D.
Baton Rouge, Louisiana

JUST AS the allergist in practice is concerned with maintaining optimum health and well-being in his patients, so is the allergist in industrial medicine concerned with maintaining optimum health and well-being in employes. Though striving for the same goal, the point of view of the allergist in industry may be somewhat different from that of his colleague in practice. The asthmatic industrial employe presents a number of problems which must be solved if he is to remain a healthy individual and an effective worker. Certain of these problems have been chosen for discussion.

OCCUPATIONAL ASTHMA

For the asthmatic who must earn a living, the job environment is of crucial importance, ordinarily second only to that existing in his home. Specific sensitization to dusts, fumes and gases may occur in any industry, resulting in conditions analogous to "baker's asthma" or "miller's asthma." Many of the important and original reports of true occupational asthma have been made by members of this Forum and its distinguished guests. Fortunately, such cases in industry-at-large are uncommon, and their resolution is simple; barring effective desensitization, the employe must be removed from his peculiarly harmful environment. Although a number of possible cases have been investigated by direct skin testing with industrial products and by observation of controlled exposures to suspected dusts or fumes, I have not yet found an example of true occupational asthma in a large refinery and pectrochemical plant with 7,500 employes.

EFFECTS OF ODORS AND SCENTS

The role of odors and scents in provoking asthmatic attacks has recently been reviewed by Dr. Ethan Allan Brown.* Gasoline fumes or other petroleum gases have been cited as asthmogenic factors in certain cases, but I have never observed this in the asthmatic employes in the refinery. When an employe alleges aggravation of an asthmatic condition by some gas or fume, I find it desirable to supplement the history by observation of an actual exposure, perhaps doing pulmonary function determinations before and after the exposure. The following is a rather extreme example in which the history alone was sufficient to rule out the alleged deleterious effect of petroleum gas.

From the Esso Standard Oil Company, Baton Rouge Refinery.
Dr. Weaver is Instructor, Department of Medicine, Tulane University School of Medicine.

Presented at the Fifteenth Annual Meeting of the Southwest Allergy Forum, New Orleans, Louisiana, May 10, 1954.

*Brown, Ethan Allan and Columbo, H. John: The asthmogenic effects of odors, smells and fumes. Ann. Allergy, 12:14-25, 1954.

THE ASTHMATIC IN INDUSTRY—WEAVER

Case 1.—A forty-year-old employe with twenty years of plant service was referred to the refinery medical department with a note from his physician requesting a job transfer because of exposure to "gases" causing the recent onset of asthma. Environmental history confirmed that he was frequently exposed to petroleum gases in low concentrations. These gases were not considered to have adverse effects upon the respiratory tract under ordinary circumstances. A detailed history of his present illness revealed that his attacks invariably began at night in his home, and that his wheezing frequently improved while on the job. Skin testing disclosed positive reactions to house dust and molds. The institution of dust avoidance and desensitization procedures resulted in immediate and gratifying relief. The employe was able to continue his regular work which he soon realized was unrelated to his medical condition.

EFFECTS OF PRIMARY IRRITANTS

Industrial dusts and fumes which may act as primary irritants to the respiratory tract constitute a problem which modern industry is striving to control. As allergists, we well recognize that a slightly contaminated atmosphere which may be well tolerated by normal individuals may have devastating effects upon an asthmatic. The successful management of the allergic worker often depends upon his avoidance of respiratory irritants. The inhalation of acid fumes or chlorine gas may dramatically precipitate an attack of wheezing. Such strongly irritating substances actually do not represent much of a problem during normal plant operations, since steps have been taken to insure their control. And, the employe with asthma knows of their existence and avoids them. With milder irritants (dusts, smokes, etc., in low concentration) the cause-and-effect relationship may not be so clear; here, the use of pulmonary function tests before and after exposure may be of great help.

Case 2.—A fifty-two-year-old pipefitter, a known asthmatic, was referred to the medical department by his foreman when he protested his assignment into an area where there might be atmospheric contamination by a catalyst dust. Previous experience with this dust had indicated that it was inert and not irritating in the low concentration encountered. The patient was wheezing mildly at the time (before exposure), and ventilatory tests revealed a vital capacity of 2,200 cc and a maximum breathing capacity of 70 L/min. At our request he reluctantly agreed to work in the area on a trial basis. He remained here until the completion of his assignment six hours later, when the tests were repeated and found to be essentially unchanged (VC 2,600 cc, MBC 75 L/min). In this case it was concluded that the environment in question had no harmful effect upon the patient's condition.

JOB PLACEMENT OF THE ASTHMATIC

In the Baton Rouge Refinery an effort has been made to identify all significant respiratory irritants and to define their areas of exposure. It is thus possible to "restrict" the asthmatic employes from conditions which we consider harmful to them. For administrative purposes, the employe with asthma is considered to have a permanent partial disability, and his job assignment is handled in a manner completely analogous to that of other handicapped employes such as amputees or "cardiacs." In order to

achieve proper placement in a job, the asthmatic employe is individually considered. For the young employe with short company service, it is desirable to recommend reassignment into some field where exposure to respiratory sensitizers and irritants, and other adverse environmental conditions (excessive cold and humidity), can be avoided or minimized. A worker should not be permitted to continue in a type of work which clearly jeopardizes his future health and well-being. The proper role of the physician is to advise both management and the employe of the consequences of continuing in such an assignment, and to make recommendations based on sound medical knowledge which point to a solution. Surprisingly, it is often difficult for the employe to comprehend that such advice is for his benefit and advantage. The problem of placement of the older, long-service employe (who may have developed asthma of the "intrinsic" type) may be equally complex. A radical change in job may deprive him of the opportunity to utilize long-acquired skills and experience. Usually, it is possible to make the necessary changes within a given craft, as by changing the worker from an "exposed" to "unexposed" location, from an "outside" to "inside" assignment, from a physically "active" to "inactive" job.

Case 3.—A forty-eight-year-old electrician first came to our attention when he suffered an asthmatic attack on the job following exposure to "acid fumes" (sulfur dioxide and trioxide gases). History revealed that he had been having occasional attacks of asthma for six years and that his attacks usually followed respiratory infections. Cutaneous tests with a selected group of antigens were negative. Ordinarily, his work was out-of-doors, and his assignments might include any unit or area in the refinery. After discussing his condition with management, it was possible to arrange a fixed job in an air-conditioned shop where the employe was fully effective with little subsequent sickness.

It is, of course, imperative that the employe's effectiveness on the job be maintained, since almost nothing leads to quicker mental and physical deterioration of the elderly employe than the feeling that he is being "placed on the shelf," or being "carried" by other more able employes.

Allergists have long recognized the necessity of investigating the working environment of their patients, and I am sure that all of you are now well aware that industry, instead of constantly perpetrating a villainous pollution of the atmosphere, in many cases provides a nearly ideal environment for asthmatic patients. We at the Esso Refinery in Baton Rouge feel particularly fortunate in this regard, for conditioned, filtered air is supplied not only to the major office areas, but also to the large shop where most of the mechanical craft work is done, and to other work areas. Progress is even being made in air conditioning some of the control rooms on refinery units. Consequently, we have a number of dust and pollen sensitive employes whose only relief during periods of respiratory distress comes when they are on the job.

DISABILITY ABSENTEEISM

For the asthmatic employe to be an effective worker, it is important that every effort be made to minimize his disability absenteeism. This requires the concerted effort of all parties concerned. The employe must have proper motivation, co-operate fully in his treatment, and take proper care of himself. The private physician must provide thorough diagnostic and therapeutic measures. And the plant physician must help by advising proper job placement, and by providing prompt and effective treatment of asthmatic attacks occurring on the job. It is exceedingly distressing to me still to see disabled asthmatic employes whose only treatment consists of an antihistamine pill or some "asthma cigarette.' I can assure you that the physician in industry is highly interested in seeing that allergic employes get the proper care which can be furnished best by a competent allergist. We are all familiar with cases of disgruntled, sick employes with extensive absenteeism who have been converted into effective workers with good sickness records by proper management of their allergic condition.

Case 4.—A thirty-eight-year-old laborer had experienced increasing asthmatic attacks for approximately ten years. Most of his treatment had been self-administered, and he had never been under the care of an allergist. Cutaneous tests were done in the refinery medical department, revealing positive reaction to antigens of the ragweed group and house dust. He was referred to another allergist for treatment, and had an excellent clinical response. During the two years prior to the institution of therapy he had been absent from work due to asthma or allied conditions on sixteen occasions for sixty-five days. In the two years after treatment was started, he experienced only four absences totalling fifteen days attributable to his allergic condition.

DISABILITY RETIREMENT

Finally, I would like to deal briefly with the matter of premature retirement. Disability retirement is never indicated in uncomplicated bronchial asthma, which is a paroxysmal disease characterized by periods of disability alternating with periods of well-being. It is only in the relatively few respiratory cripples, due to emphysema and chronic pulmonary disease associated with asthma, that premature retirement can be rationally recommended. In such cases we always like to document the degree and irreversibility of disability by serial pulmonary function studies.

SUMMARY

The asthmatic who is employed in industry represents a challenge to both the physician in practice and the physician in industry. Careful, objective tests and observations are required to evaluate properly the effects of the working environment upon his disease. The proper placement of the asthmatic employe in his industrial assignment is an important factor in preserving his health and effectiveness as a worker.

Post Office Box 551

EOSINOPHILIA IN CHILDREN

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IN TWO previous publications[1,2] the syndrome of visceral larva migrans was described. This was the term chosen to designate the clinical symptom-complex resulting from infections of the human viscera by the larvae of nematodes normally parasitic to lower animals. Subsequent reports[3,5] from widely scattered areas of this country have indicated that this syndrome is probably the most important single cause of a sustained high eosinophilia in children, with or without accompanying constitutional symptoms. The finding of the larvae of *Toxocara canis* in the reported cases and its definite identification established, in effect, a new disease. Prior to our first publication there was no authentic case report of this nematode infecting man. In fact, it was generally believed that the human was largely immune to infection by these particular parasites. Typical forms of parasitism, as ascariasis, differ from the syndrome of visceral larva migrans in many important respects.

Personal inquiries from practicing veterinarians indicate that approximately 90 per cent of dogs under the age of two years harbor the parasite *Toxocara canis* with little known detrimental effect, presumably since the dog is the natural host, although massive infections may occasionally kill the puppy. The cosmopolitan distribution of the dog ascarid and the close association of children with dogs suggested that infection of numerous children was highly probable.

Since eosinophilia is a prime feature of visceral larva migrans a consideration of the causes listed in Table I reveals the fact that the most pronounced eosinophilia occurs in patients who are infected with animal parasites which actively invade the tissues.

CLINICAL OBSERVATIONS

The syndrome usually occurs in children ranging from eighteen months to six years of age, during which time children are most likely to swallow dirt. Most of the children reported by us have been "dirt eaters." The dirt may contain ova of either human or animal parasites, or both. After a relatively short incubation period the larvae penetrate the intestinal wall and are carried via the blood and lymphatics to the various tissues of the body. Since the liver is the first natural barrier, many parasites localize there. Constitutional symptoms are protean and consist of

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TABLE I. CAUSES OF EOSINOPHILIA

Disease	Degree of Eosinophilia
1. *Allergic Disorders*	Slight to moderate
Bronchial asthma	
Urticaria	
Hay Fever	
Löffler's Syndrome	
2. *Skin Diseases*	Slight to moderate
Pemphigus	
Exfoliative dermatitis	
Dermatitis venenata	
3. *Certain Infections*	Slight to moderate
Scarlet fever	
4. Hodgkin's Disease	Slight to moderate
5. *Miscellaneous Diseases*	Slight to moderate
Sydenham's chorea	
Erythema multiforme	
6. *Parasitic Infections*	Moderate to severe
Trichiniasis	
Schistosomiasis	
Filariasis	
Ancylostomiasis	
Strongiloidiasis	
Ascariasis	
Visceral Larva Migrans	Moderate to severe

malaise, fever, pallor, loss of appetite, and muscle aches and pains. In addition, these children are cross, irritable, and otherwise emotionally unstable. Occasionally one sees transitory symptoms identical with those of petit mal. A distressing cough may be present and persist for weeks. An impetiginous pruritic type of skin rash, principally confined to the truck and lower extremities, may occur. Febrile episodes lasting from a week to ten days, with daily elevations to as high as 105 degrees, occur in the more heavily infected cases. Bouts of nausea and vomiting generally accompany these episodes. Jaundice of a mild degree frequently occurs. The liver and spleen may be enlarged. Abdominal distention is usually present. Examination of the chest may reveal findings suggestive of a bronchitis or bronchopneumonia. In an occasional case, asthmatic symptoms are prominent. X-ray studies of the chest may show patchy areas of pneumonitis. Generally, the pneumonitis resembles that described in Löffler's syndrome.

Examination of the peripheral blood reveals a marked eosinophilic leukocytosis with a total leukocyte count ranging from 15,000 to 80,000 cells per cubic millimeter. The eosinophilia may fluctuate between 20 to 80 per cent at different times in the same patient. Most of the eosinophils are mature, although eosinophilic myelocytes are often encountered. An eosinophilic hyperplasia is found in the bone marrow. An iron deficiency anemia occurs in the more severely infected cases. We have noted an occasional case to show a marked increase in the number of platelets in the

peripheral blood together with hyperplasia of the megakaryocytes in the bone marrow.

The clinical picture described above characterizes massive infection with these vigorous larvae. Just as striking, is the apparently healthy

HUMAN INFECTION WITH *Ascaris Lumbricoides*
(Ascarid of Man)

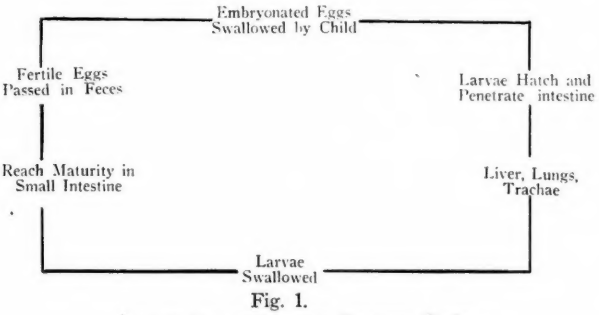
Embryonated Eggs Swallowed by Child
Fertile Eggs Passed in Feces
Larvae Hatch and Penetrate intestine
Reach Maturity in Small Intestine
Liver, Lungs, Trachae
Larvae Swallowed

Fig. 1.

HUMAN INFECTION WITH *Toxocara Canis*
(Ascarid of Dogs)

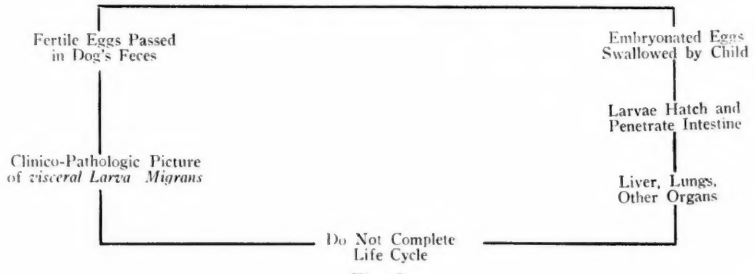
Fertile Eggs Passed in Dog's Feces
Embryonated Eggs Swallowed by Child
Larvae Hatch and Penetrate Intestine
Clinico-Pathologic Picture of *visceral Larva Migrans*
Liver, Lungs, Other Organs
Do Not Complete Life Cycle

Fig. 2.

child who, on examination, reveals nothing abnormal except a rather pronounced eosinophilia and a mild iron deficiency anemia. Apparently the degree of eosinophilia reflects in a broad sense the quantitative aspect of the parasitic infection and the allergic response of the host. Relatively light infection may be manifest clinically only by an eosinophilia. In most cases siblings who are near the same age will have an eosinophilia of a moderate degree. Generally, these children have no specific complaints other than frequent and severe bouts of "bronchitis." The clinical significance of the hyperimmune state occasioned by the presence of these parasites in the human tissue has not been evaluated.

PATHOGENSIS

After the child swallows embryonated eggs which are usually found in moist dirt contaminated with dog feces, the larvae hatch and penetrate the mucosa of the intestine. Migration then starts with most of the larvae

entering the liver. Some larvae bipass the liver and reach the lungs where they may give rise to granulomatous lesions. They may live in the human tissue for months but eventually are encapsulated by fibrous tissue and die. Figures 1 and 2 show the difference in the life cycle between human infection with *Ascaris lumbricoides* and human infection with *Toxocara canis*. While the former can eventually be diagnosed by parasitological examination of the feces for the ova of adult worms, the latter never exist in the human intestines as egg-laying adult worms since they cannot complete their life cycle in man—an unnatural host. Hence examination of the human stools for the adult worms and ova is fruitless.

PATHOLOGY

Lesions are produced by the larvae of *Toxocara canis* in the various organs of tissues to which they migrate. They have been observed so far in the liver, lungs, brain, heart, and kidney. Most of these lesions occur in the liver and lungs, as they are the first natural barriers in the migratory pathway. The larvae and their tracts are surrounded by a granulomatous inflammatory reaction. Microscopically the earlier lesions consist of an area of necrosis surrounded by inflammatory cells, mostly eosinophils and neutrophils. A single section may not show the larvae since in migrating they leave long and tortous tracts.

In order to definitely identify a fragment of larvae seen in a single microscopic section, serial sections with reconstruction of the entire parasite is necessary. Numerous microscopic sections taken from a single lesion may have to be examined before a larva can be identified.

The older lesions show foreign body giant cells, epithelioid cells, macrophages, and lymphocytes around the area of necrosis. Proliferating fibroblasts are present. Charcot-Leyden crystals are occasionally observed and a peculiar eosinophilic fibrinoid material is present in some lesions. Living larvae have been recovered from crushed preparations of fresh human brain tissue, and histologic studies of this brain showed numerous glial nodules along the paths of the larvae. Histologically, around these glial nodules in the brain one observes numerous eosinophils and a very occasional giant cell. These lesions suggest that permanent cerebral damage may be caused by these larvae and more careful consideration should be given to the cerebral manifestations and the emotional disorders of these children. It is not unlikely that heavy infections of the brain may occasionally result in dramatic neurological disorders or profound personality changes. A detailed study of the morphology of the larval stage of *Toxocara canis* has been recently done at Tulane University by Nichols.[4]

PROGNOSIS

The ultimate prognosis is good. The parasites, however, may remain active and the patient may continue to show an eosinophilia with or without symptoms for from twelve to eighteen months. The continued

ingestion of heavily polluted soil by dirt-eating children results in massive infection and the final outcome may be fatal. In the cases we have observed there has always been some other factor that precipitated death. Even children with massive infections may be expected to recover if the source of contamination is removed. It is conceivable, however, judging from the character of the tissue response—especially in the central nervous system—that irreversible changes may be produced.

DIAGNOSIS

Since dirt-eating children are apt to ingest ova of other and more familiar parasites as well, the presence of infections with ascaris, whipworm, or pinworm, for example, should not be taken as the specific explanation for a chronic eosinophilia of a high degree. Mixed infections are probably the rule. On the other hand, the failure to find parasitic ova in the stools does not rule out visceral larva migrans due to *Toxocara canis* or to some other similar parasite of lower animals whose larva is a potential invader of human tissue, but which will not complete its life cycle and mature in man, an abnormal host. Failure to find parasitic ova in the stools of such patients has led in the past to such diagnoses as Löffler's syndrome and tropical eosinophilia. Even more noteworthy is the fact that when several children of the same family all have eosinophilia which cannot be accounted for, the term "familial eosinophilia" is the usual diagnosis. In two of the families of children with positive liver biopsies showing *Toxocara canis* the siblings also had an eosinophilia. If these two children had not had severe enough infections to warrant liver biopsies in search for the cause of their illness, familial eosinophilia would have sufficed as a reasonable diagnosis. Recently I have seen one case in which the diagnosis of eosinophilic leukemia was erroneously made. It is possible that many of the reported cases of eosinophilic leukemia have been in fact visceral larva migrans even though no larvae were found in the lesions, since, as we have stated above, it is often necessary to examine numerous microscopic sections from a single lesion in order to identify the parasite. The final diagnosis of a granulomatous lesion occurring in children in which there is a pronounced eosinophilic infiltrate should be deferred until many microscopic sections of the lesion have been studied.

The pulmonary manifestations are clinically indistinguishable from those of Löffler's syndrome and tropical eosinophilia. Diagnosis must, of necessity, be clinical if there is a suggestive history, compatible physical findings, and chronic sustained eosinophilia. No skin or serological tests are as yet available.[6]

Liver biopsy, when justified, may be the only means of establishing a definite specific diagnosis by finding and identification of the specific larvae. Even when larvae are not demonstrated histologically in the granulomatous

lesion, a compatible history and physical examination may strongly indicate the diagnosis of visceral larva migrans.

The gross appearance of the heavily-infected liver at laparotomy is highly characteristic. The capsule is smooth and glistening and the organ is markedly congested. Against this dark reddish purple background numerous discreet white areas from pinpoint to 1 to 2 millimeters in diameter are strikingly visible.

TREATMENT

As yet there is no specific treatment. It is imperative, of course, to isolate the child from contaminated pets and polluted soil. It is impossible, from a practical standpoint, to kill the ova in the soil. Symptomatic treatment with vitamins, iron and short courses of antibiotics are helpful. Cortisone will usually ameliorate the symptoms and cause a temporary decrease in the absolute and relative number of circulating eosinophils. Hetrazan® has been used in large doses without beneficial effects. Arsenicals, which are said to produce good results in tropical eosinophilia, have not been tried by us but should be considered in the future.

SUMMARY AND CONCLUSIONS

In children with a high degree of eosinophilia, visceral larva migrans should always be considered in the differential diagnosis. The finding of the ova of other parasites in the stool does not rule out visceral larva migrans since mixed infections are probably the rule. Children become infected by swallowing dirt contaminated with feces of a worm-bearing dog. The larval parasites, after penetrating the intestinal mucosa, migrate to the organs and tissues producing typical lesions and stimulating pronounced eosinophilia of the bone marrow and peripheral blood. Since these larvae do not complete their life cycle in man, an abnormal host for them, egg-laying adult worms of this species are not to be found in the human intestines; therefore the specific diagnosis cannot be made by fecal examination. Liver biopsy is, at present, the only means of establishing the exact diagnosis. As yet no specific treatment is available. Awareness of the mode of infection with adequate prophylaxis against subsequent exposure is the best form of therapy.

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SOME CLINICAL PATTERNS OF BRONCHITIS

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BRONCHITIS may be defined as a superficial inflammation involving primarily the mucous membrane of the bronchial tree which frequently recurs and becomes chronic and produces the main symptoms of cough, wheezing and shortness of breath. This definition fails to indicate how variable the clinical course of this disease may be and how closely it may resemble other diseases of the bronchi.

The diagnosis continues to be popular, as is proper since the disease is common, but its atypical patterns frequently pass unrecognized. Even reliance upon its most common symptoms—cough, wheezing and shortness of breath—may lead to a breach of trust, because other diseases give rise to these complaints or may coexist with them.

Of the clinical patterns of bronchitis, that which is associated with the development of diffuse pulmonary emphysema is the most disabling and has received the most attention. But such studies are usually concerned with disturbance of pulmonary function and emphasize the bronchial factor when acute exacerbations of inflammation produce marked pulmonary insufficiency.

The development of pulmonary emphysema is an end-stage of chronic bronchitis which is difficult to understand and unsatisfying to treat. If irreversible changes in the structure of the lungs are to be prevented, attention must be given to the bronchial inflammation which almost invariably precedes and accompanies loss of pulmonary elasticity. Therapeutic efforts expended in dealing with the subacute phase of bronchitis may lead to prolonged remission.

Since our understanding of the mechanisms and pathological alterations in diffuse bronchial disease is limited, the position which the clinician assumes must be empirical but that does not preclude the possibility of making significant observations and of evaluating his therapeutic instruments objectively.

This paper will describe certain reactions of the bronchial tree to acute and chronic inflammation, illustrating the response in several instances with short case summaries. No chest x-ray films are included because attention will be focused upon bronchial factors.

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PERSISTENCE OF BRONCHITIS AFTER ACUTE ONSET

An initial episode of acute bronchitis may fail to subside despite the use of antibiotics. Such persistence is often the result of underlying hypersensitivity. Although the responsible allergen is difficult to identify, the importance of hypersensitivity in these instances is suggested by the prompt response to treatment with steroids and the poor results obtained with antibiotics.

Two cases are presented to illustrate the operation of allergic and infectious influences in patients with subacute bronchitis:

Case 1.—The patient, a thirty-nine-year-old white salesman, previously well, began to cough and wheeze in September, 1952. There was no personal or family history of allergy. He had stopped smoking in 1951. He was hospitalized for eleven days and treated intensively with oxygen, penicillin, ACTH and cortisone. He was discharged improved, but relapsed with the same symptoms in two weeks. Bronchograms done at this time were negative. He continued to cough and wheeze and occasionally was short of breath when lying down. He could work only half days. He had lost thirty-eight pounds of weight when aggravation of his symptoms in August, 1953, made rehospitalization necessary. At that time his temperature was 99.8 degrees. The respiratory rate was twenty-two at rest and marked action of the accessory muscles of breathing was present. He appeared cyanotic. Rhonchi and subcrepitant rales were heard throughout both lung fields. The white blood count was 8,000 with seventy polys and five eosinophils. X-ray films of the chest were negative. The patient coughed frequently and produced large amounts of thick mucopurulent sputum which was occasionally blood streaked. Sputum culture contained a variety of organisms commonly present in the upper respiratory tract. Penicillin and broad spectrum antibiotics produced no improvement, and Alevaire® and papain aerosols were ineffective. Cough was severe and often paroxysmal; after one spell, right lower chest pain developed as the result of a fractured rib. Hoarseness related to a nodule on the right vocal cord appeared. Scratch tests for allergy were negative. Cortisone was started after many eosinophils were found on a sputum smear. There was rapid diminution of cough expectoration and wheezing. He was discharged on the seventy-eighth hospital day. The patient has been maintained to date on 50 mg of cortisone. An episode of superimposed infection was quickly overcome with Terramycin.® Aminophyllin now relieves severe wheezing. The patient breathes more easily and misses only one day of work a week.

It seemed that infection was responsible for the large amounts of thick yellow sputum produced by this patient and prolonged treatment with various antibiotics was carried out. Cortisone was started only after a sputum smear prepared with Wright's stain demonstrated large numbers of eosinophils. Brief remissions in the past could not be evaluated because too many agents had been given simultaneously. At present cortisone has markedly reduced the patient's symptoms and exacerbations due to spasm and infection can be controlled with bronchodilators and antibiotics.

Case 2.—The patient, a thirty-six-year-old farmer, had a past history of epilepsy. He does not smoke. No personal or family history of allergy was elicited. He had no respiratory troubles until June, 1953, when he developed a nonproductive cough, shortness of breath and right anterior chest pain on the fifth day after the onset of

an upper respiratory infection. Three weeks later he became acutely ill and required oxygen. In August, 1953, he was hospitalized for shortness of breath and fever. A chest film showed scattered pulmonary infiltrations. During a hospital stay of sixty-eight days there was little response to treatment, which included penicillin, streptomycin, Pyribenzamine,® ACTH and cortisone. When he was transferred to another hospital in October, 1953, his temperature was 100 degrees, respiration twenty-eight, and blood pressure 120/70. He complained of shortness of breath and right chest pain. There was moderate cough productive of scanty mucopurulent sputum. Expiration was difficult and prolonged. Wheezes and fine rales were heard throughout both lung fields. Chest x-ray showed streaky infiltrations which disappeared in three weeks. While fever persisted leukocytosis of 19,000 was present; polys ranged up to 83 per cent and eosinophils on one occasion rose to 20 per cent. At one time blood CO_2 was 39 meq. A muscle biopsy was negative. Treatment with bronchodilators and O_2 was ineffective until penicillin was reintroduced. Fever subsided two weeks after admission. Symptoms of wheezing and nonproductive cough persisted and were relieved but not abolished by cortisone. He remains improved but still has attacks of wheezing and coughing. These are relieved by Adrenalin® and aminophyllin but sometimes respond to placebos. Though functional overlay magnifies complaints and symptoms, there is definite aggravation of patient's illness when cortisone is discontinued. He receives a maintenance dose of 50 mg. of cortisone.

It was difficult in this case to separate the factors of infection and hypersensitivity. Cortisone was not effective until the obstructive bronchopneumonia was overcome. Once infection had subsided, the clinical picture was that of bronchial asthma.

RECURRENT PULMONARY INFECTION

Localized.—Patients with recurrent bronchopneumonia restricted to the same lobe form a small, but definite class. When those suffering from obstruction of a lobar bronchus or from underlying bronchiectasis are excluded, an interesting and difficult group of cases remain. Some are true asthmatics but others appear to have a local superficial fault which predisposes to reinfection. The underlying mechanism is not clear but it seems likely that damage produced by an original inflammatory change is responsible. Such patterns of reinfection have been noted in other areas, such as the skin, and may be related to impairment of lymphatic drainage.[2] It is possible that latent foci, which contain bacteria, reactivate, but the clinical course is usually that of a descending infection of the respiratory tract. The prolonged improvement which occurs when antibiotics are given would suggest that hypersensitivity plays a neglible role in these cases.

Asthmatics with recurrent pneumonia may respond only gradually to antibiotic treatment. Evidence of bronchial spasm is usually obvious and the sputum is often scanty and tenacious. Hypersensitivity and bronchial plugging must be treated as well as infection in order to secure a complete clinical response. Frequently as in Case 2, infection must be overcome before the allergic state can be effectively managed.

The following case illustrates the course of recurrent localized bronchopulmonary infection in a nonallergic individual.

Case 3.—A forty-year-old Negro longshoreman, unemployed because of chronic alcoholism, has had episodes of respiratory infection since childhood. The attacks occur during acute changes of weather and are more frequent and severe during the winter. They begin with coryza which is soon followed by cough productive of purulent sputum and shortness of breath. There is no personal or familial history of allergy; the patient does not smoke. He is usually free of symptoms between attacks but each episode may last several months. He has been rehospitalized on many occasions complaining of productive cough, fever and left lower chest pain. Blood streaked sputum has been frequent and brisk bronchial hemorrhages have occurred. Rales are heard at the left base posteriorly. On each occasion chest films have shown bronchopneumonia of the left lower lobe with apposition of the blood vessels of the affected lobe. The infection promptly responds to penicillin. Bronchograms have been normal; injection of the mucous membrane of left lower lobe bronchus was the sole positive bronchoscopic finding in 1951. During attacks the white blood count has risen to 13,000; no increase in eosinophils has been demonstrated. The cycle of recurrent infection persists but the only evidence of reduced function is the complaint of dyspnea on exertion.

Not Localized.—A case of recurrent infection in an allergic patient is cited here to illustrate the clinical picture of obstructive bronchopneumonia complicating bronchial asthma.

Case 4.—A thirty-two-year-old white woman, a hospital attendant, has had recurrent fever and right chest pain since the age of seventeen. Her father and brother have asthma, but all tests for allergy in her case are negative. She complained only of sneezing and wheezing between febrile episodes until 1953, when she noted that she was "a little shortwinded" on exertion. Her attacks are usually associated with changes of the weather. Conjunctivitis often precedes respiratory involvement. At first dry cough and wheezing are present, but as the episodes end, she brings up a cup of thick yellow sputum daily. Blood streaking has occurred on several occasions. X-ray films taken during attacks do not always show evidence of pneumonia. Those pneumonias which have visualized have not recurred in the same zones. Bronchoscopy and bronchograms have shown no abnormalities. During febrile episodes the white blood count rises to 13,000 to 17,000 with 80 polys, but eosinophils have never been elevated. Penicillin therapy has always been associated with prompt improvement.

Although recurrent infection has always involved the right chest, the pneumonias do not recur in the same sites. A local fault has never been demonstrated. Direct evidence of allergy is lacking in this case but the family history and the interval symptoms indicate that the patient's basic disease is bronchial asthma. The bronchopulmonary infections are dominated by bronchospasm with retained secretions and do not resemble descending suppurative bronchopneumonia.

BLEEDING IN BRONCHITIS

Blood streaking and brisk hemorrhages are common in patients with bronchitis and bronchopneumonia. Forceful and paroxysmal coughing

undoubtedly precipitates many of these episodes. Bleeding occurs from a superficial erosion of the bronchial mucous membrane which is swollen, injected and friable in these diseases. It is sometimes possible to see the erosion if bronchoscopy is carried out early. Biopsies taken under such circumstances in two recent cases showed loss of epithelium and marked infiltration of the subepithelial tissue with inflammatory cells.[1] One episode of bleeding during the course of bronchitis or bronchopneumonia should cause little concern if a careful general examination has been carried out, but persistent streaking or bleeding calls for a very careful investigation of the bronchial tree and lungs to rule out neoplasm and other ulcerative processes. The essential procedure is bronchoscopy which may locate lesions that have not produced visible radiographic changes.

DYSPNEA IN BRONCHITIS AND BRONCHOPNEUMONIA

Shortness of breath frequently develops abruptly in patients with acute bronchitis. Narrowing of the bronchi by edema and cellular infiltration and obstruction of the lumen by thick secretions multiplies the resistance to the flow of air and greatly increases the amount of work required for pulmonary ventilation. In subacute and chronic cases, the same pattern is seen when new acute infections occur. However, in such patients, the factors producing increased resistance to air flow are always present and the respiratory work required for moderate exertion will often result in breathlessness.

The following case illustrates the difficulties which are encountered when severe airway obstruction is present in the course of acute diffuse bronchopneumonia.

Case 5.—A thirty-four-year-old Negro housewife was hospitalized in March, 1951, complaining of shortness of breath for one week. There was no previous history of respiratory disease or personal or familial allergy. Her illness began with rhinorrhea, headache and cough. On the second day chills, fever and right chest pain developed. Sputum was mucopurulent and occasionally blood streaked. Temperature was 103 degrees on admission, the respirations were forty and shallow. The tonsils and pharynx were injected. Moist rales and wheezes were heard throughout both lung fields. White blood count was 14,300 with 82 per cent polys, and seven eosinophils. Various α-hemolytic streptococci were obtained from sputum culture. The chest film taken on admission showed miliary bronchopneumonia. Treatment was begun with penicillin and oxygen, and fever fell promptly, but spontaneous cough was ineffective in raising the thick mucopurulent sputum and tachypnea persisted. The patient was encouraged to cough more deeply. Large amounts of purulent sputum were obtained and respiration became normal. Since discharge on the fifteenth hospital day, she has had no respiratory complaints to date.

In this case airway obstruction persisted after the infection had been controlled by antibiotics and was finally relieved by mechanical measures. In some instances the introduction of a tracheal catheter for suction and to promote cough by irritation may be required. Where cough is ineffective in the face of accumulating secretions, tracheotomy will be necessary.

This procedure should be used when the patient is senile, disoriented, comatose or suffers from a neuromuscular disorder, such as poliomyelitis or myasthenia gravis.

Secondary changes in the lungs which aggravate dyspnea in these cases may be mentioned at this time. Multiple check valve mechanisms within affected small bronchi and bronchioles will result in areas of obstructive pulmonary emphysema which may be visible on chest films as thin walled pneumatoceles. These zones are poorly ventilated and the blood which perfuses them returns to the left heart with a low content of oxygen. To maintain minute oxygen consumption in the face of impaired gas exchange increased pulmonary ventilation and blood flow are necessary. The increase in respiratory rate and volume intensify dyspnea because of the greater amount of work required to overcome the resistance to air flow within the bronchial tree and the difficulty encountered in ventilating overinflated lungs.

Fortunately, the secondary pulmonary changes are reversible and disappear when the obstruction within the airway is relieved. The importance of oxygen therapy during the stage of obstruction must be emphasized, because higher concentrations of oxygen will reduce the ventilation required. As a result respiratory work and dyspnea will be diminished and physical exhaustion prevented.

SUPERIMPOSED BRONCHITIS

True bronchitis with the common symptoms of cough, wheezing and shortness of breath, usually following coryza, is often superimposed upon other diseases affecting the bronchial tree. If a complete history and physical examination are not carried out, the underlying disease may remain undiscovered for long periods of time.

Congestion of the lungs and structural alterations and bronchial deformities predispose to repeated superficial bronchial infections. It is not uncommon to encounter a patient with unrecognized mitral stenosis who has been called bronchitic or asthmatic for many years. An adequate history and physical, radiologic, and fluoroscopic examination will establish the presence of this condition. Diseases like progressive sarcoidosis which distort the structure of the lungs are often complicated by recurrent bronchial infections. Chest films taken in asymptomatic intervals will demonstrate persistent infiltrations and permanent alterations. There will frequently be evidence of extrapulmonary involvement and an informative biopsy can often be obtained.

The possibility of irreversible destructive disease of the bronchi should be considered in all of these cases. Diffuse bronchitis may complicate localized bronchiectasis which is suitable for surgery. The discovery of localized rales in a symptomless interval and radiographic evidence of persistent focal infiltration or contracted lung will be sufficient indication for bronchographic examination.

CONCLUSION

The diagnosis of infectious bronchitis may be difficult because of variations in clinical course and the atypical prominence of individual symptoms. The clinical picture of allergic bronchitis may resemble that of infection and frequently both processes coexist. The separation of the two factors is essential for early effective treatment and will spare the patient symptomatic discomfort and in some cases may prevent or arrest tissue damage where symptoms are intermittent. Careful study of the patient during the attack will usually determine whether he suffers from fundamental structural or allergic disease. This information will be valuable in treating and arresting recurrences in the future.

The possibility of underlying cardiac or pulmonary disease must always be considered and sought for. A careful history and a complete physical examination will usually reveal additional findings in patients who suffer from bronchitis engrafted upon other diseases. A negative chest x-ray film will almost invariably exclude all important diseases of the heart and lungs. Rarely, bronchogenic carcinoma will exist in a superficial infiltrating form which only later becomes visible radiologically. In such patients, however, the symptoms are intractable and persistent blood streaking is present.

The prognosis in patients with acute and subacute bronchitis is uncertain. Where an allergic component exists, exacerbations may be expected. A symptom-free interval does not guarantee that infection will not recur. The severity of the original episode is of little prognostic value; severe suppurative bronchopneumonia may subside without residua, while a troublesome "chest cold" which did not require hospitalization may persist in the face of all treatment.

As long as the pathogenesis of infectious bronchitis remains speculative and we have no clear idea of the influences responsible for the persistence, recurrence and progression of this disease, treatment will be only symptomatic and preventive measures which limit bronchial irritation and infection will be the strongest defenses against this common disease. Further insight into the mechanisms which produce the variable patterns of bronchitis is essential for more precise diagnosis and rational treatment.

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CLASSIC ASPECTS OF ONION AND GARLIC DERMATITIS IN HOUSEWIVES

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CONTACT dermatitis of the hands in housewives constitutes a common and difficult diagnostic problem. Its frequency has been augmented in recent years by the increasing variety of objects coming in contact with the hands, including the newer plastic materials and more efficient detergents. Recognition of certain distinctive anatomic patterns facilitates early diagnosis. The value of such landmarks has been emphasized in the monographs of Waldbott[16] and Ronchese[11], who have compiled lists of the more common patterns. The present report concerns an additional distinctive pattern which I have observed and studied during the past ten years in the fingers of housewives as a result of contact with onions or garlic.

Onions and garlic are members of the *Liliaceae*, a family closely related to the *Amaryllidaceae*, which includes narcissus, daffodil, campernelle, jonquil, polyanthus, and chinese sacred lily, and to the *Iridaceae*, which embraces iris and gladiolus. Although plants of the lily family are not common irritants, they are known sensitizers. Derbes[3] reported a case of hay fever and asthma caused by narcissus bulbs, and Henson[7] described another in which powdered garlic was the responsible agent. "Tulip fingers," according to Bertwistle[1], occur in 85 per cent of the workers in Holland. "Lily rash" is common in the Scilly islands, where vast numbers of narcissi are grown. In the United States, as well as in Europe, dermatitis has been traced to hyacinths, and Stryker[12] found jonquils to produce dermatitis in flower growers of this country. Garlic has been known to cause the phenomenon of cutaneous sensitivity either by its bulb or by its pollen.[13] In a case reported by Burgess,[4] dermatitis of the fingers and palm of the left hand in a cook resulted from paring onions and garlic. Edelstein[5] described dermatitis of the wrist in a meat grinder after he had rubbed this area against debris containing garlic.

The following description of a case, the first observed by me, is typical of this syndrome.

REPORT OF A CASE

F. M., a thirty-seven-year-old white woman stenographer, had an eruption of the tips of the thumb, index, and middle fingers of the left hand as well as the tip of thumb of the right hand. (Fig. 1). Exacerbations and remissions had alternated continuously for several years. There was no family history of allergic diseases.

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Invariably, the eruption was worse on Monday mornings and actually began to flare up on Saturday nights. Detailed questioning regarding possible contact agents in her office and home yielded no pertinent information. She could think of nothing she touched with these three fingers of her left hand that did not come in contact

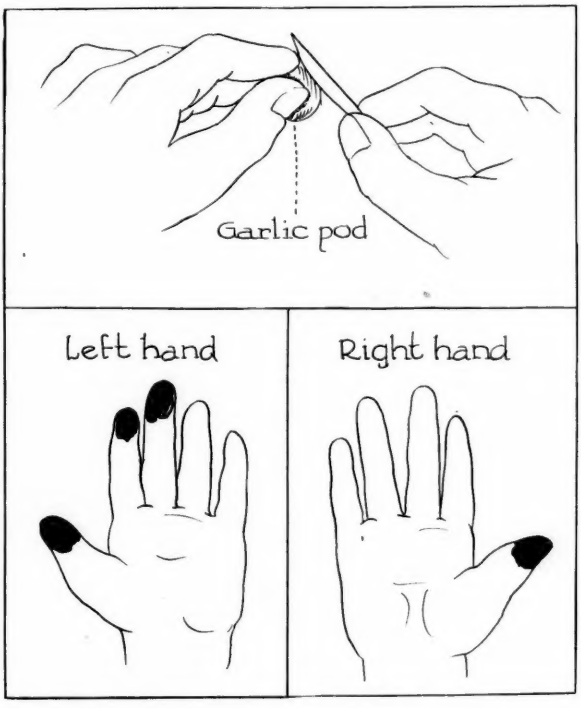

Fig. 1. Characteristic distribution of onion and garlic dermatitis of the hands of housewives. Note eruption on the tips of the thumb, index, and middle fingers of one hand and the tip of the thumb of the other.

with her right hand, for she was right-handed. Further questioning revealed that she was fond of cooking but, because of the nature of her occupation, dined in restaurants on weekdays. On Saturdays, she prepared her own meal, usually roast beef, which she seasoned with chopped onions and garlic. These she held with her left thumb, index and middle fingers while she chopped with a knife held in the right hand, the lateral radial aspect of the right thumb hitting the chopping board with each stroke.

Patch tests were made by applying cut, raw surfaces of onions and garlic to the volar aspect of the left forearm near the wrist. Within twenty-four hours a severely pruritic vesicular dermatitis appeared. Reaction to garlic was more severe and was prolonged to three weeks. Areas of dermatitis of the fingers flared during patch testing.

Avoidance of further contact with onions and garlic through use of protective

creams and gloves, along with soothing local treatment of the dermatitis, effected complete remission. Three months later, she had another attack after planting lily bulbs. Patch test to the cut, raw surface of this bulb yielded a positive reaction. On another occasion she attributed a flare up to ingestion of garlic in a salad, but no intradermal testing was done.

COMMENT

Since this initial observation, numerous similar cases have been recognized. In one patient, a housewife, the reversal of localization to the left thumb and the right thumb, index and middle fingers was due to the fact that she was left-handed. In another instance, the left-handedness of a patient was accurately predicted from these clues.

Because onions and garlic are used so extensively for seasoning in Louisiana, as in other southern states, the incidence of this type of dermatitis is much higher in these areas. It is common practice for the housewife to hold the bulb of these plants against a chopping board with the thumb, middle and index fingers and to hold the knife in the opposite hand, the blade being grasped by all fingers and the handle extending across and beyond the palm. As she chops, the lateral radial aspect of the thumb hits the chopping board and the chopped substance. Another technique consists in holding the pod between the thumb, index and middle fingers of one hand and paring against the thumb. When large onions are used, the contact pattern follows a distribution which coincides with the points of contact made by holding a ball in the hand. Waldbott[16] has classified this localization as a "finger grip type" of pattern, arising from gripping such articles as knobs, office equipment, kitchen drawers, metal or plastic bottoms, small pieces of jewelry, lipstick containers, pills, tablets, popcorn, peanuts, and olives. In these instances, however, three digits of the right hand and one of the left are usually involved because of the predominance of right-handedness, whereas the onion and garlic pattern commonly occurs on the three digits of the left hand, which hold the plants.

PATCH TESTING

Earlier, Edelstein[5], Burgess[4], and others applied the cut, raw surfaces of onions and garlic to the unbroken skin of the wrist of patients with this pattern and obtained positive reactions, the severity in some cases suggesting the action of a primary irritant. Several years ago I used the irritant action of onion to produce vesiculation for treatment of "creeping eruption." In one such patient, patch testing to onions three weeks after cessation of treatment with onion poultice yielded a negative reaction. Apparently, the irritant action varies with the potency of certain varieties of the plant.

Extracts were prepared in an effort to eliminate the possibility of primary irritation and to discover which fraction (oil or water soluble) was the offending allergen. Fifteen grams each of onion and garlic were

TABLE I. RESULTS OF PATCH TESTING WITH ONIONS AND GARLIC

Type of Dermatitis	Water Soluble Fraction Reactions				Fat Soluble Fraction Reactions				Total Number Subjects
	Onions		Garlic		Onions		Garlic		
	Neg.	Pos.	Neg.	Pos.	Neg.	Pos.	Neg.	Pos.	
Onion and/or garlic dermatitis	6	4	2	8	9	1?	9	1	10
Unclassified eczematoid dermatitis of hands	3	2	3	2	5	0	5	0	0
Control	10	0	10	0	10	0	10	0	10

chopped separately and macerated with mortar and pestle and were placed in separate filters. Five ounces of ether in one case and five ounces of water in the other were poured over each of these. This filtrate was used in full strength for testing. The volar surface of the left wrist was cleansed with soap and water. An elastoplast type of patch with a central protective area of cellophane was applied over a bit of cotton saturated with the extract. Twenty-four hours later, patches were removed, except in a few cases in which almost immediate reaction took place. Readings were made at twenty-four, forty-eight, and seventy-two hours, and reactions were graded from one plus to four plus. One four plus reaction persisted as a localized dermatitis for three weeks. Of the last ten patients tested, one had a one plus reaction to the fat soluble extract of garlic and a questionably positive reaction to that of onion. Eight exhibited from two to four plus reactions to the aqueous extract of garlic, four of whom also had positive reactions to aqueous extract of onion (Table I).

An equal number of control subjects with no history of dermatitis was tested, all of whom had negative responses. Of five patients with unclassified eczematoid dermatitis of the hands, two demonstrated two plus reactions to the aqueous extract. Both of these had complained of burning of the hands after contact with onions and garlic. From these results it is apparent that the allergenic substance is water soluble.

DISCUSSION

The foreign literature contains contradictory reports regarding the actual mechanism of dermatitis produced by the lily family. Touton[14] incriminated a parasite in the cloves of garlic, but Overton[10] exonerated *Leptus autumnalis* as a cause for lily dermatitis. Earlier, in cases of hyacinth and tulip dermatitis, the traumatizing action of sharp-edged crystals of oxalate of lime was suspected and was found to be eliminated by treatment of the plants with weak hydrochloric acid. Hoffman[8] considered the sensitizing agent to be not a glucoside but an etheral oil. Touton,[14] Broers,[2] and Freeman[6] believed this oil to exist only in the juice of fresh bulbs of the tulip, whereas Kranenburg[9] and Waanders[15] found the offending substance in dry hyacinths. Touraine and Neret's[13] patient was sensitive both to the raw fresh bulbs and to extracts, and, in their

article on occupational tulip dermatitis, they concluded that the theory of parasites and crystals must be discarded.

The odor of onions and garlic has been found to be due to essential oils, in onions mainly allylpropyl disulphide, which also appears in small amounts in garlic along with the main constituent of diallyl disulphide. In addition, these plants contain other sulphur-bearing oils of unknown chemical composition. The coexistence of positive reactions to onions and garlic would tend to suggest an offending oil common to both.

SUMMARY

A hitherto unreported distinctive pattern of contact dermatitis of the hands of housewives due to onion and garlic is described, involving the thumb, index and middle fingers of one hand and the thumb of the other. Studies with raw and extracted substances of these plants indicate an allergenic as well as a primary irritant action. Contrary to previous reports, the allergenic extract was found to be water soluble rather than fat soluble.

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THE RELATIONSHIP OF BACTERIAL INFECTION AND RESPIRATORY ALLERGY

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THE RELATIONSHIP of bacteria and respiratory allergy has been a problem discussed for a long time. Whether bacteria is a cause of respiratory allergy or an aggravating factor has had its champions on each side of the question. For the most part, conclusions have been drawn from clinical impressions.

In the literature, conclusions have been drawn concerning the effectiveness of penicillin, sulphonamides, and other antibiotics in the prevention and treatment of respiratory allergies. Since we have not been able to draw conclusions from our clinical and blind use of antibiotics in this field of work, we have tried to evaluate the relationship of bacteria and allergy from a more scientific point of view.

Before speaking of the abnormal, we must first consider the normal findings. The normal nasal cavities, sinuses, and bronchial tree are sterile. The bacterial flora which exists is isolated to the nasopharynx. When the antibacterial barriers are broken by lowered resistance of the nasal mucosa, the bacteria from the nasopharynx spread into the nasal cavities, sinuses or bronchial tree. Secretions from the normal upper respiratory areas may have small but insignificant numbers of nonpathogenic bacteria which are of no real significance. The common nonpathogens are *Staphylococcus albus, Staph. aureus b, diptherioids, Neisseria pharynges, and Staph. aureous A.* If spreads of such secretions show no micro-organisms, or just a few, and a large amount of mucus, then the evidence is strong that one is dealing with a vasomotor disorder. Stained smears of secretion examined under a microscope will give a clear-cut picture of whether an allergy, infection, or a combination exists. Pneumococci, *Streptococcus hemolyticus, Hemophilus influenzae* and *parainfluenzae,* and *Klebsiella pneumoniae* are found very rarely in the normal nose or sinus even in small numbers. The finding of such organisms even in small numbers strongly suggests the presence of infection.

One of the most significant manifestations of nasal, sinus or bronchial disease is a discharge of secretions. This material may vary considerably in consistency, color, and amount. The color or amount of secretions in itself is not diagnostic of infection, no more than a cloudy urine is indicative of the presence of white blood cells.

After such an examination to determine whether an infection, allergy, or a combination is present, cultures should be made to determine the or-

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MICROSCOPIC FINDINGS

	Cytology
Normal nose	No or few micro-organisms Mucus 0 to 2 plus Polys. 0 to 1 plus
Allergic rhinitis, sinusitis, or bronchitis	No or few micro-organisms Mucus 3 to 4 plus Usually eosin. to 4 plus Occas. polys. alone
Nasal, sinus, and bronchial infections	Micro-organisms often 3 to 4 plus Mucus 0 to 2 plus Polys. to 4 plus
Allergic rhinitis with infection	Micro-organisms 3 to 4 plus Mucus to 3 or 4 plus Usually eosins. to 4 plus Polys. to 4 plus

ganism causing the infection. Sensitivity studies are then essential to find the specific antibiotic which will eradicate the infection. These procedures are simple and can be carried out in the office with little trouble and less expense. In our experience with sensitivity tests, we have found that the correlation of these tests and clinical results have been almost perfect.

In our office laboratory, we kept records of 200 consecutive sensitivity tests, made from patients with respiratory infections. The findings were of great clinical significance.

1. Penicillin was specific in 10 per cent of the cases.
2. Streptomycin was specific in 33 per cent.
3. The combination of penicillin and streptomycin was specific in 30 per cent of the cases where both penicillin and streptomycin were negative. Therefore, the combination of penicillin and streptomycin had some degree of specificity in 73 per cent of the cases.
4. Chloromycetin was 80 per cent specific.
5. Aureomycin was 60 per cent specific.
6. Terramycin was 70 per cent specific.
7. Erythromycin was 34 per cent specific.
8. Sulphonamide was 8 per cent specific.

Since this series of tests, we have completed a few hundred more, of which accurate records were not kept. Generally, one can say that the low rate of penicillin and sulphonamide specificity has become still lower, as well as the percentage of specificity of the other antibiotics. Therefore, more and more, it has become essential to do sensitivity tests before any extensive therapy of infections. This technique of examination of the secretions and sensitivity tests was applied to a series of 227 cases of non-febrile upper respiratory infections of children under two years of age. In the majority of cases the children were under one year of age.

In these 227 cases, the cytological examinations showed that sixty-six children (29 per cent) were sterile; and of these fifty-eight (88 per cent) showed abundant eosinophils; 161 (71 per cent) were infected, and 103 of these (64 per cent) showed 2 plus to 4 plus eosinophils.

From this series, it appears that allergy is a factor in a majority of nonfebrile respiratory infections during infancy, if the presence of eosinophils is of any real diagnostic significance. In a significant number of these cases, sooner or later, there was clinical evidence of allergic disease.

In a group of 113 sterile and non-sterile patients who received no therapy, fifty (44 per cent) were well within fourteen days, or an average of nine days, while sixty-three (56 per cent) were not improved after fourteen days. In fifty-eight sterile cases which were followed, twenty-nine patients were free of symptoms within fourteen days (an average of nine days) and the same number still had symptoms after the two-week period. Of fifty-eight infected patients given some non-specific therapy or no therapy at all, one-half (twenty-nine) were free of symptoms within fourteen days, an average of eight days, and the other twenty-nine still had symptoms after fourteen days. Thirty-three patients without eosinophils, or with only a few, were followed without therapy with almost identical findings.

Nineteen infected patients were given antibiotic therapy after fourteen days of symptoms, and of these seventeen (89 per cent) were symptom-free within four days, while two patients (11 per cent) were not cured of symptoms but were sterile within four days.

Specific antibiotic therapy was given to ninety-two infected persons, whose symptoms were from eight to fourteen days' duration, and of these fifty-nine (64 per cent) became symptom-free, while thirty-three (36 per cent) had no clinical results but were sterilized.

The foregoing findings may be summarized as follows:

1. As manifested by the presence of eosinophils, allergy is very common in the upper respiratory infections of infants under two years of age.

2. Infections prevail in the majority of respiratory disturbances in this age group.

3. Approximately 50 per cent of the upper respiratory infections became clinically cured within an average of eight days without specific therapy.

4. Specific antibody therapy sterilized all the infections and helped to attain a clinical cure in 64 per cent of the patients whose symptoms were from eight to fourteen days' duration.

Of 175 patients with routine cases of nasal and bronchial allergy, ages ranging from two to eighty years, one hundred (57 per cent) were sterile and seventy-five (43 per cent) were infected. This is in contrast to those under two years of age, which group showed 71 per cent infection and

29 per cent sterility. Apparently, infection is common in the majority of allergic respiratory infections in the lower age group of infants, and uncommon in the older group of children and adults.

Frequently and consistently, we find that many allergic infants cease to have symptoms of allergy after two years of age. For this reason we limit, for the most part, any specific therapy in this group of infants. After they become two years of age, we stress specific allergic investigation and therapy. From our limited investigation, we feel that since infection is so common in the first years of life, it is a marked aggravating factor in the field of allergy rather than a specific cause. Again, the rapid growth of the body in the first two years of life may cause physiologic changes which decrease the number of infants with allergic symptoms which persist after two years of age.

In a special group of 100 patients, from two to eighty years of age, suffering from nasal allergy, asthmatic bronchitis and bronchial asthma complicated by infection, specific antibiotic therapy was instituted with the following results:

1. Of thirty-two patients with allergic sinusitis complicated by infection, twenty-two (70 per cent) showed good results, while ten (30 per cent) showed no results.
2. Bronchial asthma with infection was present in thirty patients, of whom seven (23 per cent) showed good results, while twenty-three (77 per cent) showed no results. .
3. Of thirty-eight patients whose asthmatic bronchitis was complicated by infection, twenty-three (60 per cent) showed good results and fifteen (40 per cent) showed no results.

SUMMARY

1. Infection is much more frequent in allergic respiratory infections in patients under two years of age than in the older group of children and adults.
2. Favorable results are obtained with the use of specific antibiotics in allergic conditions complicated by infection.
3. Bronchial asthma with infection is the least influenced by the use of specific therapy of the infection.
4. In no case studied could infection be labeled as a specific cause of the allergy.
5. In many cases infection could be considered as an important secondary factor or as a trigger mechanism to precipitate or aggravate an existing allergy.

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LONG-TERM ANTIMICROBIAL THERAPY IN ASTHMA ASSOCIATED WITH INFECTION

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AN INCREASING number of patients with wheezing or symptomatic asthma without demonstrable allergic sensitivity has come to our attention. Many of these patients undoubtedly have chronic low grade respiratory infections. It has occurred to us that since adequate treatment of known chronic infections, such as tuberculosis and actinomycosis, have necessitated long range antibiotic therapy, the same might be true in asthma associated with infection.

Antibiotics have been successfully used in asthma associated with acute respiratory infections.[1] The literature abounds with the importance of the role of infection in acute asthmatic episodes in children.[2,4] Fishman[5] reported the successful use of a sulfonamide mixture in the prophylaxis of recurrent infective asthma in twenty patients who failed to respond to allergic or other treatments. The decrease in upper respiratory infections has been previously well demonstrated in patients with rheumatic fever.[3,7]

It is often difficult to establish the most important factor in an individual asthmatic episode. In such a case are we dealing with a superimposed infection or a demonstrable clinical allergy? Cultures of these secretions will show bacteria varying as to species, season and virulence.[6] For this reason, cultures have not given consistent results.

METHODS AND MATERIALS

The data collected on each patient consisted of an allergic survey, including history, physical examination, skin tests, chest and sinus x-rays, nasal smears for eosinophils and Gram stains of sputa.

The pulmonary function was evaluated both before and during therapy by subjective information from the patient, followed by chest examination, and finally by determining the vital capacity and maximal breathing capacity.

Treatment consisted of various combinations of the following for periods ranging from three to eighteen months:

1. Procain penicillin in 300,000 to 600,000 unit doses 3 times weekly.
2. Streptomycin 0.5 Gm or dihydro-streptomycin 0.5 Gm 3 times weekly.
3. Gantrisin® in doses of 1.0 Gm 3 times daily.

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4. Bicillin® 600,000 units every one to two weeks.*

The results of this study are given in Table I.

CASE SUMMARY

R. L., a white woman, aged thirty-nine, had a history of rhinitis and bronchitis for many years. At the age of thirty, she had had left pulmonary tuberculosis and spent two years in a sanatorium. At the age of thirty-four, she had bronchiectasis of the left lung (Figs. 1 and 2), and at thirty-four a left pneumonectomy. She also had asthma which was worse during the winter associated with U. R. O.'s. At thirty-eight, she missed three months' work during the winter. At thirty-nine, she showed sensitivity on intradermal testing to house dust, alternaria, feathers, dog. She was hyposensitized. She was treated with 600,000 units of Bicillin every two weeks. She also had Gantrisin on three occasions. She missed only three days' work during the winter (Fig. 3). Pulmonary function is summarized in Chart 1.

DISCUSSION

In a study of twenty-three patients treated for periods ranging from three to eighteen months, we believe we can justifiably state that the great majority received considerable benefit from both a therapeutic and prophylactic standpoint. Several chronic intractable asthmatic patients with varying degrees of status, who were constant visitors to the emergency room, have had long remissions under the treatment outlined. In the majority of the patients, both the number and severity of attacks decreased while on therapy.

Of the antibiotics used, all were effective. It is obvious that no single antibiotic will be effective in all respiratory infections. At best, the number and severity will be reduced. In patient R. L., Bicillin was given every two weeks, while three short respiratory episodes were treated with Gantrisin. In a busy clinic, there is some value to a therapy which may be given every two weeks.

We are well aware of the possibilities of complications of antibiotic therapy, the most feared of which is anaphylaxis. Only one mild reaction to penicillin was noted. This was primarily dermatitic and occurred after three months of therapy. Considering the large number of injections in hypersensitive individuals, this is not excessive.

It was not our purpose to make bacteriological surveys of the effects of antibiotics on respiratory flora. This has been performed by others with varying results. It was our purpose to determine if long-range antimicrobial therapy is of benefit in the prophylaxis and therapy of asthma associated with infection.

Doubtless many of the so-called pulmonary cripples with emphysema, fibrosis, and bronchiectasis have arrived at this state of pulmonopathy for want of a previous adequately sustained therapeutic effort. It is, of course, much too early to determine the value of long-term anti-microbial

*This material was generously provided by Pfizer & Co., Hoffmann-La Roche, Inc., and Wyeth & Co.

TABLE I.

Patient	Age	Symptoms and Duration	Skin Tests	Treatment	Results
J.L.J.	34	Asthma, 7 years	Grass +, ragweed +	Desensitization, DHS and Penicillin for 3 weeks. No further medication.	Good
I.G.	49	Asthma and nasal obstruction, 39 years	Feathers + +, orris root + +, house dust + + + +	Desensitization, DHS and Penicillin intermittently for 1 year	Status quo on desensitization; excellent on antibiotics
B.H.	24	Asthma, 10 years	Questionable	DHS and Penicillin 3 x weekly for 1 month	Good (VC 1100 and 2000; MBD 20,000 and 42,000
B.C.	28	Asthma and nasal symptoms, 11 years	Questionable	Desensitization to house dust DHS and Gantrisin 3 x weekly	Questionable Excellent
L.W.	24	Asthma, 15-20 years	Negative	DHS and Penicillin for 2 months	Fair
A.M.W.	47	Asthma, 30 years	Negative	DHS and Penicillin for 3 months	Excellent
E.H.	50	Asthma, 6 years (Emphysema)	Negative	DHS and Penicillin for 3 months	Moderate improvement
T.H.	59	Coughing and wheezing, 4 years (Emphysema)	Negative	Penicillin 500,000 u 3 x weekly for 3 weeks	Fair
B.M.	4	Asthma, 1½ years	Grass +, house dust +, alternaria +	Penicillin 600,000 u 3 x weekly for 2 weeks	Good
P.S.	63	Asthma, 16 years (Emphysema)	House dust ±	Penicillin 500,000 u daily for 2 weeks; then 3 x weekly for 2 weeks	Improved
P.C.	9	Asthma and intermittent nasal symptoms, 6 years	Questionable	Penicillin 500,000 u 3 x weekly for 1 week; 250,000 u orally 4 x daily for 2 weeks	Excellent
R.F.	6	Asthma, 4 years, purulent sputum	House dust ±, alternaria ±, yeast ±	Bicillin 600,000 u every 2 weeks for 3 months; desensitization to house dust and alternaria	Good
W.S.	36	Asthma, 32 years (according to parents)	Negative	Penicillin and DHS 3 x weekly for 1 month	Fair
G.H.	27	Asthma, 24 years	Questionable to house dust	Penicillin 300,000 u 3 x weekly for 3 months; Gantrisin 15 grains 4 x daily for 6 weeks	Poor
J.M.	53	Asthma, since infancy; purulent sputum daily for 3 years	House dust + +, feathers + +	Terramycin during hospitalization; Bicillin 600,000 u every 2 weeks for 2 months	Fair
P.H.	5½	Asthma, 3 years	Alternaria +, house dust +	Desensitization; Penicillin 500,000 u 3 x weekly for 2 weeks, 1 x weekly for 6 weeks	Excellent
M.B.W.	50	Asthma, 6 years every night	Negative	DHS and Penicillin 3 x weekly for 3 weeks	Excellent
E.M.K.	37	Asthma, 5 years	Questionable to house dust, grass and careless weed	Desensitization; DHS and Penicillin 3 x weekly for 4 weeks	Questionable to desensitization; excellent to antibiotics
O.B.	50	Asthma, 4 years	Ragweed +, tobacco +	Gantrisin 1 gram 4 x daily for 3 weeks	Good
D.G.	46	Asthma, 20 years	Negative	DHS and Penicillin intermittently for 4 months	Excellent
L.E.	65	Asthma, 30 years	Ragweed +, careless weed +, mattress dust + +	DHS and Penicillin 3 x weekly for 3 months	No recurrence
M.K.K.	66	Asthma, 25 years; hay fever, 45 years	Ragweed + +, house dust + + + +, elder +	Gantrisin 1 gram 4 x daily for 1 month; Penicillin and DHS 3 x weekly for 1 month	Good
D.S.	7	Asthma, 3 years	Grass +, house dust +, careless weed +	Gantrisin 7½ grains 3 x daily for 2 months Maintained Bicillin for 2 weeks	Good

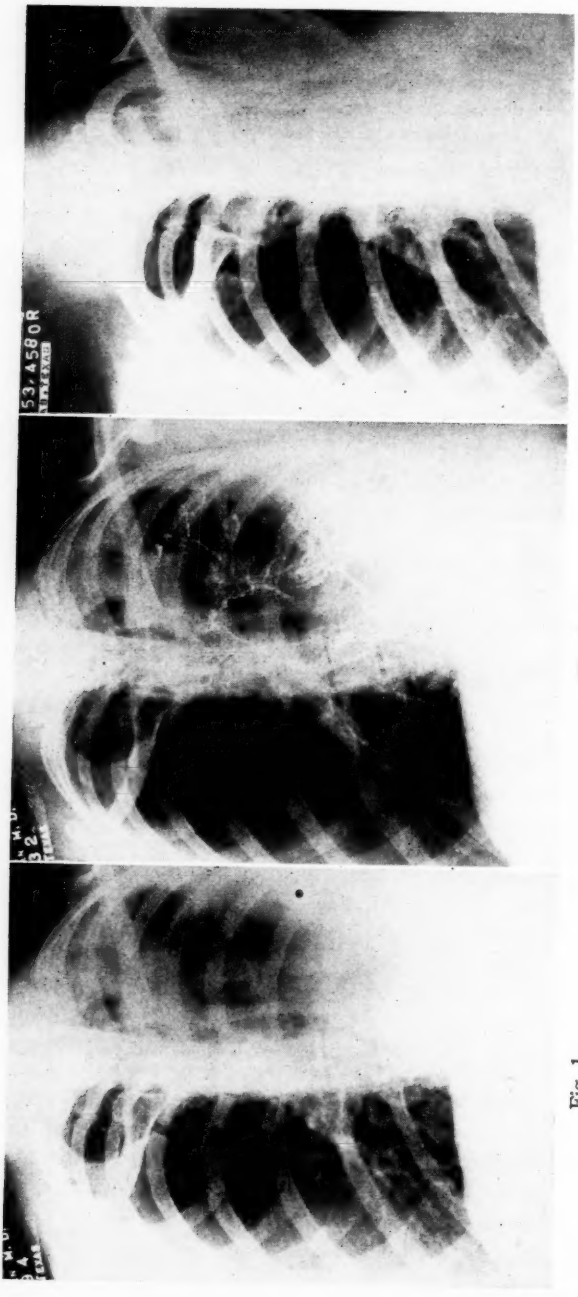

Fig. 3

Fig. 2

Fig. 1

therapy in the prevention of such pulmonary crippling. However, it would seem that this is a logical approach.

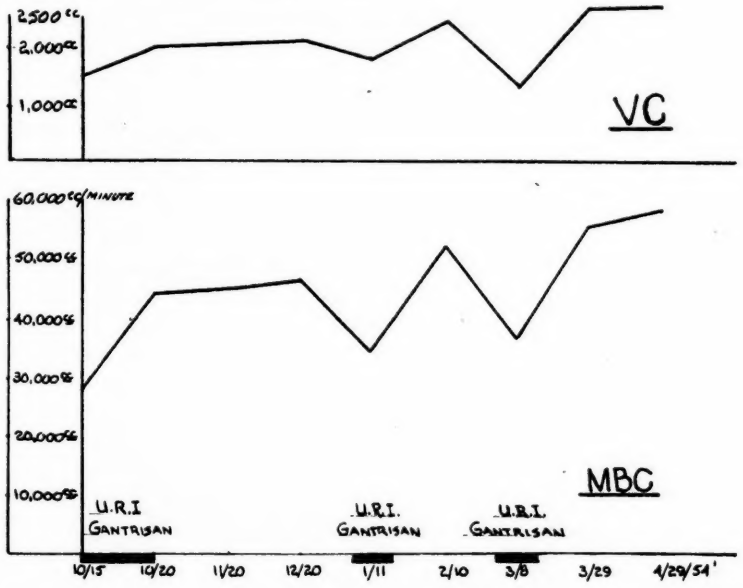

Chart 1. Patient R. L.—Increase in pulmonary function (vital capacity and maximal breathing capacity) while on Bicillin (Wyeth) 600,000 units every two weeks.

SUMMARY

1. Twenty-three chronic asthmatic patients were treated with continuous anti-microbial therapy for periods ranging from three to eighteen months. Of these, sixteen obtained excellent results, four obtained moderate improvement, two showed slight improvement, and one showed no improvement.

2. In the great majority no allergy could be demonstrated.

3. One mild reaction to penicillin was noted.

4. The number and severity of the asthmatic attacks were lessened.

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ANTIBACTERIAL THERAPY IN INFECTIOUS ASTHMA

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ANTIBACTERIAL therapy in the treatment of infectious asthma is in essence the therapy of the infection responsible for the onset of the asthmatic seizure. The present concept of antibacterial therapy received its first impact with the introduction of the sulfonamides, and has continued with the newer antibiotics. Regardless of their differentiation into chemotherapeutic and antibiotic drugs, the principle of their action is antibacterial in that the therapeutic effect is the result of either their bacteriostatic or bacteriocidal action on the flora of the infection.

Therapy of infectious asthma with antibacterial drugs is not new. The various derivatives in the sulfonamide group of drugs have been rather extensively investigated as a means of controlling the infection in these cases. In 1946 penicillin, the first of the modern antibiotics, became available in sufficient quantities for clinical evaluation. Following in the order of their discovery, almost all of the antibiotics have been studied and clinically tried in the treatment of infectious asthma. A review of the reports of the cases of infectious asthma treated with antibacterial drugs either therapeutically or prophylactically, indicates that they have been of definite value in many cases. An analysis of the cases which have not responded satisfactorily to the antibiotic does not justify condemnation of the principle of antibacterial therapy in infectious asthma.

The problem as it presents itself should not necessarily be concerned with establishing the value of antibacterial therapy in the treatment of infectious asthma, for the results have been sufficiently good to justify its inclusion in the present armamentarium of the allergist. The problem of antibiotic therapy in infectious asthma, on the other hand, should be concerned with studying the factors in those cases in which it has not been of value. An analysis of the possibly significant factors in those cases which failed to respond to antibacterial therapy must include studies concerned with establishing criteria for diagnosis of infectious asthma. The significance of the various bacteria of the flora in the infection responsible for an asthmatic attack is of utmost importance. The various factors of antibacterial therapy must be established on a laboratory basis in order to permit the selection of the proper antibiotic.

Infectious asthma probably exists in two forms: the perennial and more common form, in which the infection precipitates the attack, and the type in which asthma exists only at the time of an acute infection.

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Bupert states that in his opinion infectious asthma is that in which infection is almost solely the responsible agent, including all cases in which asthma responds little if at all to the conventional antiasthmatics or any of the routine antiasthmatic procedures. Prigal feels that the diagnosis of the importance of infection in infectious asthma will depend upon three points: (a) the history of an infection with attacks of asthma; (b) presence of infection in the respiratory passages; (c) laboratory confirmation of the infection in relation to the asthma. He states that the diagnosis of asthma *per se*, unless of the infected or mixed type, is not an indication for antibiotic therapy, nor should treatment of asthma be limited to the treatment of infection, since it is well known that other specific allergens or psychogenic factors, or both, can aggravate this condition. Of these two conceptions as a basis for establishing the etiology of infection in infectious asthma, the criteria of Prigal is more inclusive and more positive in its approach. In instances infection may only contribute a precipitous factor in cases of infectious asthma. The simple control of an infection in these cases would be of less value than in those cases in which infection was the sole cause of the attack. Therefore, in certain cases it might be necessary to use a combined form of therapy, one directed against the infection, the other being antiasthmatic in its effect.

In those cases in which the infection is either the sole or contributing cause of the onset of the asthmatic attack, it is of utmost importance that bacteriologic studies be made to determine the species of bacteria present. References in the literature to the bacteriology in cases of asthma clearly indicate that in the majority of cases the infection is one resulting from a mixed flora of bacteria. Theoretically it is highly possible that only one of the recovered species is the etiologic pathogen, the other species exerting a saprophytic role in either the infection or the precipitation of the asthma. In cases with a mixed bacterial flora it is impractical if not impossible to determine the etiologic significance of any of the recovered species. Therefore, considerations in antibacterial therapy should include determinations of the antibacterial effect of these drugs against all species recovered. In the majority of cases studied bacteria of the Gram-positive group, principally those of the streptococcus, micrococcus, and pneumococcus groups, have been most frequently reported. However, there are instances where other organisms, including many of the Gram-negative group as well as others still less common, such as the Friedlander bacillus, have been reported.

The relationship of the various species of bacteria in an infection caused by a mixed flora of bacteria will be the same in cases of infectious asthma as it is for other infections not necessarily related to this condition. In many cases only one of the species will be pathogenic, whereas in others any or all of the species may be individually pathogenic. There are other cases in which the infection is the result of the sum total of the pathogenic properties of two or more of the species present. A synergistic

relationship between the bacteria often exists and is capable of producing an infection differing from that which would result from the pathogenic activities of the species acting independently of each other.

In vivo studies of the pathogenicity of the bacteria recovered from infections with a mixed flora have confirmed these different relationships of the flora to the infection from which they have been recovered. Meleney described a synergistic relationship found in the cases of chronic synergistic gangrene of the skin. This lesion is the result of a synergistic action between a micro-aerophilic non-hemolytic streptococcus and a hemolytic *staphylococcus aureus*. Both species are pathogenic in themselves, but the infection resulting from their synergistic action differs pathologically and clinically from that which would result if either were individually responsible for the infection.

In 1951 several cases of infection resistant to accepted theories of therapy, including use of almost all antibacterial drugs, were studied and found to be the result of synergistic action of the species in the flora. All bacteria recovered from the discharges, sinus tracts and cavities of these infections were injected in pure cultures and in various combinations subcutaneously in guinea pigs. These animals were observed for the development of infection which occurred only when two or more of the strains were injected as a single inoculation.

A discussion of the various components of an infection as possible allergens precipitating an attack of asthma is only of academic significance. It is of little clinical importance whether it results from an exotoxin, endotoxin, bacterial protein, split protein resulting from enzymatic or fermenting action, or from any other part of the infection. The allergen responsible for the attack of asthma could be multiple but would not exist except to support a theory that the bacteria themselves could be the allergen. However, there is no proof that under certain conditions they will not have certain allergic tendencies. It therefore becomes self-evident that antibacterial therapy should be effective in cases of infectious asthma if the therapy employed is effective against the infection responsible for the asthma.

The site of infection usually associated with cases of infectious asthma is in the respiratory passages, including those of the upper respiratory system as well as those of the deeper bronchi and terminal bronchioles. However, it is academically debatable whether, if the infection is acting as an allergen in precipitating the asthmatic seizure, that infection with similar features elsewhere in the body might be capable of causing an asthmatic seizure.

Except for certain known features of infections peculiar to the respiratory system, the antibacterial therapy of these infections follows the same rationale as for infections elsewhere. The anatomy of the respiratory system lends itself both to the parenteral and topical routes in antibacterial therapy, the topical route being in the form of aerosols.

If one is to be guided in the choice of an antibiotic or antibacterial agent in the therapy of infections by the species sensitivity of bacteria to anibiotics, a rationale for its selection must be based upon the knowledge of the species of bacteria causing the particular infection under consideration at that time. Antibiotic sensitivity tests against various strains of a single species of bacteria have shown that within the species individual strains will enjoy a wide range of sensitivity levels. The range of sensitivity between strains of staphylococci recovered from staphylococcal infections to penicillin illustrate these variations in sensitivity to the same antibiotic. The range includes those which are sensitive to concentrations of penicillin as low as .015 units per cubic centimeter of volume, as well as those which are completely resistant. Studies with the other antibiotics have demonstrated that this principle of strain variation in antibiotic sensitivity holds for all antibiotics against their strain of the species in their respective flora. Those antibiotics enjoying a rather broad species of antibacterial spectra are principally of the tetracyclin group, which includes Aureomycin,® Terramycin,® Achromycin,® and Tetracyn.® Streptomycin has rather wide antibacterial spectra, but for the most part its main activity is limited to the Gram-negative strains of bacilli being moderately effective against the Gram-positive cocci, and showing some inhibitory action against the acid-fast bacilli. Penicillin and bacitracin, on the other hand, are principally effective against the Gram-positive cocci, but its antibacterial spectra will include a few other species of bacteria, as well as some of the spirochetes. The antibacterial spectra discussed refer to the antibiotic effect on strains of bacteria recovered mainly from infections in surgical patients. The spectra of the various antibiotics in non-surgical infectious diseases are equally well known, and the same limitations and usefulness of these antibiotics in these medical infections holds as it does for the surgical infections.

At present the only rationale which is reasonable in antibacterial therapy has to do with the familiarity of the expected etiologies and the knowledge of the range of action of the antibiotics against these expected etiologies. With this knowledge an initial selection of an antibiotic can be made in the absence of laboratory confirmation which, if obtainable, is time consuming. In many localities the lack of adequate facilities prohibits the titration of antibacterial-antibiotic sensitivity. Whenever possible, specimens for bacteriologic study and antibiotic sensitivity tests should be obtained for the analysis at the onset of therapy. Bacteriologic analysis of these specimens should identify the species of bacteria present in the flora of that particular case. Sensitivity tests should be made with all of the antibiotics against all of the strains recovered. This knowledge will then be available in the event that the antibiotic selected on clinical grounds should prove to be ineffective in any given case.

The principles outlined concerning rationale in the approach to antibacterial therapy in infections should hold equally well for treatment of

the infection in cases of infectious asthma as it does for other types of infections regardless of its location in the body. There is one difference, however, in cases of infectious asthma, in that the infection is usually not so acute as to require that the antibiotic be given prior to the laboratory test, which might shed more light on the nature of the strains of the bacteria causing the infection. With information obtained from the laboratory a more rational selection of the most likely antibiotic is possible. Therapy in the absence of this information permits a big element of chance in the selection of the antibiotic, the continuation of which is suggestive of empirical medicine.

Inasmuch as infectious asthma is a chronically recurrent type of disease, additional supportive therapy to increase resistance to infection, as well as possible immunological therapy in selected cases, should be considered essential. Also the etiology of each episode of infection causing recurrences of asthma may not necessarily be the same in each instance. The type of infection, as well as the bacteriology occurring with each episode, will often differ. Therefore, it cannot be assumed that because a particular antibiotic was effective on one occasion it will necessarily be effective in a later recurrence. Each episode should be considered as an individual and specific infection receiving the same bacteriologic studies of its flora and of the sensitivity of the flora to the various antibiotics.

In conclusion, it might be reemphasized that the infection which precipitates the seizure in those cases of infectious asthma should not differ significantly from an infection elsewhere in the body. If antibacterial therapy directed against the infection in these cases is to be effective in controlling or stopping the asthmatic seizure, it must be specific against the infection for each seizure in every case. Failures of this form of therapy being reported in the literature can in part be attributed to one or more of the following: (a) an inaccurate evaluation of the significance of the infection as the cause of the asthmatic attack; (b) failure to administer an effective antibiotic against the particular infection against which it is being used; and (c) failure of an effective antibiotic to reach the site of the infection.

It should be remembered that antibacterial therapy in the perennial type of asthma referred to in this paper is less effective when compared with the same form of therapy in those cases in which each asthmatic attack is dependent upon a new and acute infection.

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ALEVAIRE INHALATION FOR ELIMINATING SECRETIONS IN ASTHMA, SINUSITIS, BRONCHITIS AND BRONCHIECTASIS OF ADULTS

A Preliminary Report

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ALEVAIRE® is a mucolytic aerosol detergent solution. It has been used by inhalation to dissolve bronchial secretions and to moisten mucous membranes in a great many respiratory conditions in infants and children.[2,4,9,12,13,14,16,19,20] It is also of value in anesthesiology[17,18] to prevent and relieve post-operative atelectasis and pneumonia.

Alevaire is particularly effective in children with bronchial obstructions characterized by thickened mucous and mucopurulent secretions. Its effectiveness in children naturally led to its empirical use in similar conditions in adults.

Bronchial asthma, sinusitis, bronchitis and bronchiectasis are very common in adults and are characterized by viscid mucopurulent secretions. There has been no satisfactory method in the past for eliminating these secretions in the sinuses and bronchi, and a tremendous amount of literature attests to the fact that they are responsible for a great deal of prolonged symptomatology, complications, and sequelae.

Furthermore, the bronchospasm and wheezing of chronic asthmatics is often not the primary difficulty but is the result of a reflex set up by the presence of irritating bronchial secretions. Removal of these secretions eliminates not only the cough, but the reflex bronchospasm (and dyspnea) as well. Thus it is possible in some cases to relieve completely a prolonged asthmatic attack by the simple inhalation of a suitable detergent aerosol.

Alevaire inhalation is also a rational approach to chronic sinusitis and sinobronchitis, and their later sequel of bronchiectasis. The thinning and washing out of the thick secretions in the sinuses and bronchi not only relieves symptoms temporarily, but often terminates the entire attack.

The group of patients herein reported was not studied as a research program. The work with adults began purely spontaneously as a supplement to a more closely controlled study in children.[14]

TECHNIQUES OF ADMINISTRATION

Two techniques of administration were employed: (1) Tent method for overnight therapy (Fig. 1), (2) Direct application of the nebulizer

Presented at the Fifteenth Annual Meeting of the Southwest Allergy Forum, May 11, 1954, New Orleans, La., by Dr. Joseph B. Miller.

Dr. Miller is an Associate Fellow of the American College of Allergists.

Alevaire® is supplied by Winthrop-Stearns, Inc., New York 18, N. Y.

Fig. 1. Tent method for continuous or overnight therapy at home. Note that the top is entirely open.

equipped with a nasal tip to the external nares for short periods of therapy (Fig. 2).

The most severe cases were treated overnight while sleeping. These patients continued their daytime activities as usual so that their treatment did not interfere with their normal routine. On going to bed at night they simply switched on their compressors and climbed into their tents. On arising in the morning they simply switched off their compressors and went about their usual activities.

For the patients receiving overnight treatment the equipment consisted of an air compressor, a 500 cc nebulizer, a home-made tent and a 3-foot length of ½ inch inner-diameter gum rubber tubing connecting the nebulizer with the tent (Fig. 1). The tents employed were wooden or metal frames with plastic or cotton materials forming the four sides of the tent. The top of the tent was left open to minimize the feeling of claustrophobia so common in asthmatic patients, to allow for the escape of body heat, to obviate the necessity of a cooling mechanism and to provide a foolproof source of air in case of power failure.

Most of the severe cases receiving overnight therapy in a tent were able to change within a few days to the second technique of direct application of the nebulizer. The second technique was, therefore, employed in

severe cases after they no longer required tent therapy and in milder cases from the beginning of treatment. Some severe cases preferred to continue the use of the tent for convenience (rather than changing to direct nasal application) as it did not encroach on their daytime activities.

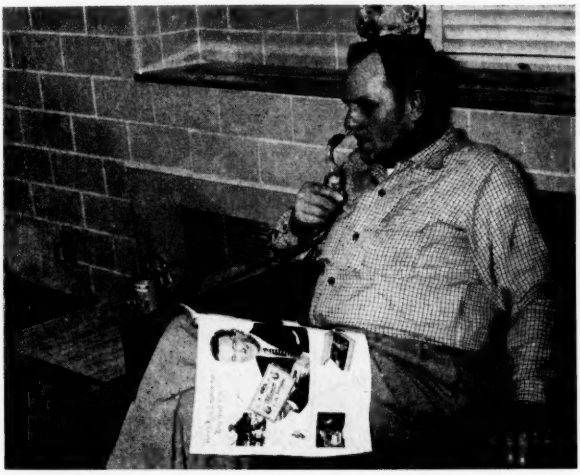

Fig. 2. Direct application of the nebulizer, equipped with nasal attachments, to the external nares for short periods of therapy (usually one hour).

The second method of administration consisted in the inhalation of the Alevaire aerosol mist by holding the nebulizer directly to the external nares. Some patients took their treatments in the office and others bought equipment for home use. The equipment for this technique consisted of an air compressor, a DeVilbiss No. 40 nebulizer plus No. 40 TR nasal adapter (available in a single package, as the DeVilbiss No. 640 combination) and a 4-foot length of 3/16 inch inner diameter rubber tubing connecting the compressor to the nebulizer (Fig. 2).

Alevaire was originally available only in 500 cc bottles, but it may now be obtained in 60 cc bottles. This is more convenient for the second method of administration. The DeVilbiss No. 40 nebulizer will conveniently hold 10 cc (approximately 2 teaspoonfuls of Alevaire) which will last for about forty to sixty minutes when nebulized at an air pressure of 10 pounds per square inch. The patients in this group were given one-hour treatments once or twice a day. When the patients became virtually free of symptoms they were allowed to reduce the duration of treatment as desired. After one or two weeks most of these patients reduced treatment to thirty minutes a day taken at bedtime. Most

were finally able to stop treatment altogether except when they contracted a new respiratory infection or felt that an attack of asthma was beginning.

The vast majority of patients prefer to inhale aerosol through the nose rather than through the mouth. Prolonged mouth breathing and prolonged

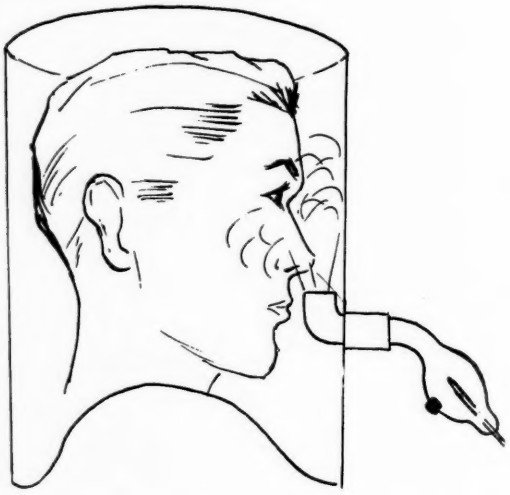

Fig. 3. Administration by a face hood, made of transparent plastic. Other hoods and masks are also applicable.

forceful breathing are fatiguing as well as irritating to the throat. Every patient is instructed to breathe the aerosol through his nose and to breathe perfectly normally without any attempt to increase the depth of inhalation. The patient should also be warned not to overexert at the first treatment and to discontinue the treatment temporarily if he becomes tired. Many of these patients are already weak and dyspneic and any additional effort may cause fatigue and resistance to further treatment. It is well understood that deeper breathing deposits more droplets in the depths of the lungs, but results are regularly obtained without this strain. Moreover, the patients' comfort and co-operation are essential. Each patient must be handled individually, but must not be allowed to have complete control of treatment. The treatments should be rapidly lengthened to approximately one hour at a time to obtain maximum benefit, because a patient who continues to stop treatments at the end of five or ten minutes will obtain relatively little benefit.

In the hospital oxygen may be used in place of an air compressor. Oxygen should be employed at a rate of 8 to 10 liters per minute which is approximately equivalent to 10 to 12 pounds per square inch with an air compressor. The oxygen should not be bubbled through a water bottle, as

this is unnecessary and causes loss of pressure in the line by leakage of oxygen.

For hospitals, ordinary oxygen tents are unsatisfactory for aerosol use, as the air-circulating mechanism draws the aerosol out of the tent too

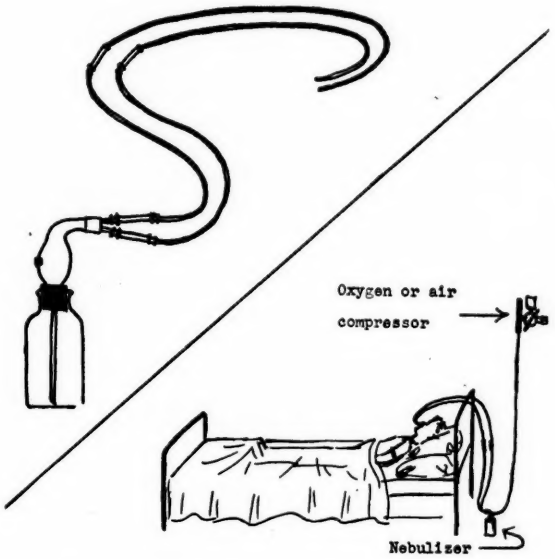

Fig. 4. Administration by nasal catheters. This is particularly suited for the severely ill hospital patient requiring oxygen as well as Alevaire.

rapidly. A suitable tent for the hospital administration of Alevaire has not yet appeared on the market. Fairly good results in adults are obtained at present by putting the patient's head in an Infant Croupette.* Although the Croupette is not made for adults, it has a cross-bar that can be loosened to open it wider for the comfort of adult patients. There is ordinarily a rain of large droplets of Alevaire from the Croupette nebulizer, so that the patient may complain of being too wet. This can be largely eliminated by the addition of a suitable baffle to the nebulizer, which allows the fine mist to enter the tent but traps out the large drops and returns them to the nebulizer reservoir.

Two additional methods of administration, although not employed in this group of patients, are illustrated (Fig. 3 and 4).

The air compressor most frequently employed in this study was the Wocher Whirlwind. Any compressor may be used so long as it produces

*Air-Shields, Inc., Hatboro, Pennsylvania.

oil-free, dust-free air at a pressure of 10 to 12 pounds per square inch, and a volume flow of 8 to 10 liters per minute. It should be reasonably quiet and light in weight, not overheat under prolonged use, and not be difficult to maintain.**

CASE REPORTS

Case 1.—J. M. was a forty-seven-year-old white man with chronic bronchial asthma, who had been in moderate status asthmaticus constantly for almost twenty years. His illness was characterized by a constant wheeze, shortness of breath, non-productive cough, easy fatigability and a constant sensation of secretions in his chest which he was unable to expectorate. His asthma was aggravated by rainy or cold weather, by the inhalation of dust (e.g. when floor was swept), by upper respiratory infections and by emotional stress. He had had bronchitis and pleurisy several times. He had sought relief from many physicians, went through an allergy clinic (which included complete allergy testing and treatment), and attended a well-known asthma clinic every six weeks for eleven months in 1952-53. He had taken almost every prescription and proprietary medicine available for asthma with only occasional diminution in symptoms. His chest x-ray was negative.

In September 1953 the patient started treatment with Alevaire by the overnight technique. During the very first night his cough became productive for the first time and upon awakening he was able to expectorate enough secretions to obtain definite relief. During the course of the first ten days of treatment his sputum changed from a thick greenish almost solid material to a thin colorless liquid. Before treatment began he had occasionally been able to expectorate a small bronchial plug by violent coughing and could push it out of his mouth into a tissue while in the supine position. As the treatment progressed, the bronchial plugs became easy to expectorate, and finally became so watery that he was forced to sit up to expectorate, and about twenty paper tissues were required per night to contain the secretions, rather than the occasional one for each night. By the tenth day the chest was almost completely free of secretions, there was no wheeze and the patient was experiencing a sense of well-being and freedom from symptoms that he had not had in many years.

After the tenth day the patient decreased his treatments to thirty minutes twice a day by direct nasal application for an additional twenty days. He finally discontinued the treatment altogether as he was completely free of symptoms and felt like a well man, except that he still had to clear his throat several times on arising and occasionally during the day. During the ensuing months the patient had experienced no further attacks of asthma although several times he had given himself a thirty minute treatment prophylactically on cold or rainy days and once during a mild upper respiratory infection. He is continuing now, eight months later, on a symptom-free status.

**Two new and better compressors have just been introduced specifically for Alevaire use. They are made by the DeVilbiss Co., Somerset, Pa.; and the National Medical Pumps and Specialties Corp., Boonton, N. J.

A new versatile nebulizer has just been introduced, and serves for both short-term (1-10 cc) or long-term (500-1,000 cc) treatments (Hiflow Nebulizer, National Medical Pumps and Specialties Corp., Boonton, N. J.). Other continuous duty (500 cc) nebulizers available are: (1) Microfier (National Cylinder Gas Company, Chicago 11, Ill.), (2) DeVilbiss No. 840 (DeVilbiss Co., Somerset, Pa.), (3) Mist-O_2-Gen (Production Foundry Company, Oakland 7, Calif.), (4) Elliot (Elliot Medical Plastics, Inc., Lynn, Mass.), and (5) IEC 500 cc Nebulaire (Inhalational Equipment Co., New York 28, N. Y.).

Case 2.—G. H. was a fifty-eight-year-old white man with chronic bronchial asthma of fifteen years' duration in moderately severe status asthmaticus. He had a constant wheeze and a persistent aggravating non-productive cough. When he was able to raise sputum, it was thick, sticky and yellowish. He had to sleep on three pillows and had to get out of bed in the middle of each night for one or two hours for almost fifteen years to be able to "catch his breath." In recent years he has had to take sedatives every night in order to sleep at all. His previous treatment consisted of expectorant cough syrups, antibiotics, bronchodilators, and sedatives none of which gave any appreciable benefit. His chest x-ray was negative.

In September, 1953, the patient started treatment with Alevaire by direct application of the nebulizer to the external nares for one hour twice a day. On the second day the patient noted that his sputum was more liquid and easier to raise. His cough was also less frequent and less severe. The breathing gradually changed from a slow, shallow, labored, and painful breathing to a deeper, "quicker" and easier breathing. The patient felt that he was able to breathe more naturally and that he could now get the air down further into his chest. The bronchospasm and wheezing began to decrease on the second day of treatment. All these symptoms gradually disappeared and in fourteen days the patient was completely free of wheeze and cough. However, he found that he could not discontinue the use of Alevaire completely without a return of symptoms and he later reverted to and is continuing the use of Alevaire for fifteen minutes each night before retiring. His secretions begin to loosen up and he can begin to cough them out within about five minutes after the completion of his treatment and in ten or fifteen minutes his chest is clear again. Now he rarely is bothered by wheezing, he sleeps all night without having to get up to "catch his breath," and he has not taken a sedative since the first night of Alevaire treatment. He sleeps now without any pillows at all and has no dyspnea. His only remaining symptom is a productive morning cough during which time he expectorates a small amount of watery secretion. Formerly this morning cough was non-productive and continued all through the day, along with a constant wheezing and a shallow labored breathing. The patient describes his improvement graphically by stating that "before I could only breathe down to here (nipple line) whereas now I can breathe all the way down to here (umbilicus)".

Case 3.—R. C. was a forty-five-year-old white man with chronic asthma of twenty-seven years duration, with wheezing, aggravating non-productive cough, shortness of breath and easy fatigability. He too had exhausted all efforts to obtain relief. His secretions were so thick that in the middle of the night he would have to get up and have his wife beat him on the back in order to free the plugs of his bronchi. Only after he coughed up these plugs could he again breathe freely.

In September, 1953, the patient started treatment with Alevaire, with two one-hour treatments the first day by direct nasal inhalation. This was sufficient to free him of mucous plugs almost completely and on the second day he cut his treatment to forty-five minutes once a day at bedtime. He continued his treatments this way for about two weeks and then discontinued his treatment altogether. By then he was completely free of wheeze, coughed only on arising in the morning and could breathe as well as he ever had before developing asthma. Whereas the sputum was originally thick, yellow, solid and often reached a volume of two cupfuls per day, it is now a clear thin liquid which is expectorated easily on arising each morning and is completely eliminated in a few minutes. His entire treatment used only about 750 cc of Alevaire. He continues to keep the nebulizer and compressor at the bedside and occasionally uses it for a few minutes before retiring, if he feels a little "choked up" with mucus, thereby preventing wheezing attacks.

Case 4.—R. M. was a thirty-five-year-old white woman with severe asthma of one year's duration and a history of severe sinus trouble and hay fever all of her life. She had pneumonia three times and had been under medical care almost constantly. In August, 1953, she suffered an acute asthmatic attack and an acute exacerbation of her sinusitis. She obtained no relief with prescribed medications.

In September, 1953, the patient started treatment with Alevaire, by application of the nebulizer directly to her nares for one hour, three times a day. After three days' treatment she had obtained only slight relief so she was put on overnight therapy. This immediately produced results and after one night she was able to raise her secretions and breathe much easier. From this first night she was able to sleep ten hours each night without sedatives, whereas previously she had used sedatives every night and obtained only partial rest. She continued overnight treatments for three weeks during which time she improved daily. She did not use the Alevaire during the daytime except on the second day of overnight treatment; she had slept so well the night before that she stayed under the Alevaire all the next day and rested. Her response was so well correlated with her treatment that when her nebulizer went out of adjustment several times in the first few nights, she would begin to wheeze and wake up. She then reset the nebulizer and after an hour or so would obtain relief and fall asleep again. At the end of the three weeks of treatment she had reached the point where she had no cough or wheeze whatsoever and even her nose and sinuses were more open than they had been in nearly a year. Her sputum had changed from a thick yellowish green semi-solid material to a thin watery liquid. Her nasal and sinus secretions underwent the same change. The volume of sputum before treatment was one cupful per day, increasing to two cups per day in the first few days of treatment and then tapering off and completely disappearing by the end of three weeks. When she reached this state of perfect freedom from sinusitis or asthma, she discontinued her Alevaire treatment. She keeps her compressor and nebulizer by the bedside but has never had to use them again. The sinusitis, as well as the asthma, has been completely relieved and she feels well in every way. This is a remarkable situation insofar as her sinuses are concerned, for she has never before gone through a winter without experiencing severe sinus trouble.

Case 5.—F. W. was a sixty-one-year-old white man who had an acute onset of asthma two months before being seen. He had received antibiotics, antihistamines, expectorant cough syrups and antispasmodics all to no avail. He had a severe wheeze, a deep painful cough and his voice was so hoarse that his initial history had to be taken in whispers. His sputum consisted of thick yellowish masses, about one cupful each day.

In October, 1953, the patient started Alevaire treatment, with the direct nasal application of the nebulizer, but instead of an air compressor he used a large bicycle pump as a source of air pressure. His treatment consisted of one hour of Alevaire inhalation twice a day. His response was definite but a little slower than the previous cases, probably due to the less efficient method of nebulization. In the first two days there was no response whatsoever, but there was partial improvement on the third day. His sputum became much thinner, more copious and easier to raise. On the fourth day it was a clear watery liquid, about a cupful in volume. In the next few days the sputum decreased rapidly in amount. By the seventh day he was completely free of sputum, cough, and wheeze, and he was breathing normally. He therefore stopped his treatment and has been virtually symptom free ever since. However, he has felt an asthmatic attack starting four times since then and each time he has avoided the attack by using Alevaire inhalation one hour twice a day for one day. He now goes about his work normally and is completely symptom free.

Case 6.—C. R. was a twenty-six-year-old white woman with bronchitis and bronchiectasis of five years' duration. She had a severe tight cough, usually nonproductive, but occasionally productive of one to two teaspoonfuls of thick greenish-yellow sputum. This cough had followed an attack of postpartum pneumonia six years ago. The cough underwent several remissions and exacerbations, during which the temperature ranged around 101 to 102 degrees for seven to ten days. The fever often declined but never disappeared completely. She often had coughing attacks lasting ten to fifteen minutes at a time. This was particularly true at night, so that she was unable to sleep. Two bronchograms were obtained and they showed definite though slight bronchiectasis. Her treatments consisted of postural drainage, penicillin, aureomycin, terramycin, and various expectorant cough syrups, with no benefit.

In December, 1952, the patient was given Alevaire inhalation by direct nasal application one hour a day for two weeks, and then one hour every other day for an additional two weeks. During this time her sputum first became a thin liquid, easy to raise, and then disappeared completely. After that time she was completely free of cough and was able to sleep all night. For an additional two months she had to resort to Alevaire inhalation again on several occasions when she felt she was catching a cold and the cough was returning. Since that time (December, 1952), she has been completely free of cough and has not had to have Alevaire or any other medication.

Case 7.—C. S. was a thirty-one-year-old white man with bronchiectasis and sinusitis, who had had pneumonia six times, the last attack on August, 1953. He had a continuous thick purulent post-nasal drip and a thick yellowish-green sputum. He expectorated at least a cupful of sputum each morning on arising. He felt weak and debilitated with frequent chilly sensations and a low grade fever. Bronchograms on two different occasions revealed severe bronchiectasis of the right middle and both lower lobes. Previous treatments consisted of antibiotics, postural drainage and expectorant cough mixtures, all without benefit.

In September, 1953, the patient started using Alevaire, with one hour of direct nasal inhalation every day for two weeks. Within a few minutes after the first treatment he expectorated a great deal of sputum and definitely breathed easier. His nasal passage, which had been almost completely occluded, also benefited from the very first treatment, and he could then breathe easier through his nose as well as his chest. The second treatment produced still further improvement in both the sinusitis and bronchiectasis. By the third day the patient was feeling stronger, eating better, breathing easily through both nares, and getting his bronchial secretions out much more easily. This improvement continued day by day and at the end of fourteen days he was almost completely free of difficulty. At that time he tried to discontinue his treatment completely but found that his secretions thickened up and that his chest would feel particularly full on arising in the morning. Therefore, he resumed the use of Alevaire for fifteen minutes before bedtime. He is now continuing to use the Alevaire every night in this manner and is completely free of symptoms except for daily morning expectoration of light, fluffy sputum.

Case 8.—A. H. was a twenty-eight-year-old white man with acute severe exacerbation of a chronic sinusitis which for nine years has grown steadily worse. When "open," his sinuses drained about ½ cupful of blood-streaked yellow material each day. His last attack was so severe that his face was very swollen and tender and he received no relief whatsoever from penicillin injections or decongestive nose drops.

In October, 1953, the patient started using Alevaire, with one aerosol treatment consisting of one hour of direct nasal inhalation. This relieved his congestion moderately and opened his nasal passages partially for the first time in several days. He

was unable to return for regular treatments, so he was then put on Alevaire nose drops which he instilled at home by an ordinary medicine dropper, using the Proetz head low position. This served to wash out his sinuses and so was continued for five days with increasing benefit each time. He found that he began to obtain relief and free drainage of material about thirty minutes after each instillation. He was then given a bottle of Alevaire containing 1 per cent Neo-synephrine.® He reported that he then obtained the same results, but obtained them within five minutes instead of thirty minutes after each instillation. He is continuing this nasal instillation as a daily regime and is controlling his chronic sinusitis well. Whereas he always had a post-nasal drip all day he now experiences it only in the morning when he first awakens and at night when he first goes to bed. Although he is not cured, he has less difficulty now than he has had in over a year.

Case 9.—H. M. was a forty-eight-year-old white man with chronic bronchial asthma, bronchiectasis and emphysema of six years' duration with remissions and frequent acute exacerbations. In September, 1953, he had an acute asthmatic attack which could not be relieved by ordinary bronchodilator aerosols or by different types of bronchodilator capsules. He had used cortisone for a previous attack and had obtained some relief, but this attack did not respond to cortisone at all. He was wheezing severely, coughing and expectorating two cupfuls of a yellow sputum daily.

In September, 1953, the patient started using Alevaire by direct nasal inhalation for one hour daily for one week. In the middle of his very first treatment he began to expectorate the sputum that had been so troublesome and each day the sputum became thinner and easier to raise. At the end of a week of treatment he was able to sleep all night without sedation for the first time in months. He was also able to sleep flat on his back whereas for the previous three years he had had to sleep sitting up in a chair. His sputum volume was decreased to about one or two teaspoons daily and is now a thin foamy liquid.

He is free of wheeze but still has some rhonchi in his chest. However, he has been much stronger and has gained seven pounds in the two months since instituting treatment. He still uses Alevaire about once a week when he begins to feel that he is filling up with secretions. The most striking benefit of his treatment is improved physical stamina. Previously he had difficulty doing a full day's work without great fatigue and he was unable to rest at night. Now he sleeps well and accomplishes his day's activities with markedly greater ease and less fatigue. It is probable that he would obtain even greater relief by using Alevaire more regularly, but he is a busy executive and does not feel able to take time out for treatment except when practically incapacitated.

Case 10.—C. M. W. was a seventy-year-old white man with chronic sinusitis, emphysema and bronchiectasis. The bronchiectasis is severe and widespread, involving bronchi in every segment of both lungs. He has had as many as eight attacks of pneumonia in one year. As he has been dyspneic all his life, with symptoms extending back to infancy, and has been diagnosed by his physicians as having congenital bronchiectasis. The dyspnea becomes worse in attacks and is precipitated by the mildest exertion as well as by the inhalation of cool air, including air-conditioned air. He also had a cough during this entire time, felt choked up, but was never able to bring up any sputum. He has been progressively worse in recent years, and was finally confined to his room where he sat propped up in a chair most of the time.

When the patient was offered Alevaire therapy, he was too easily fatigued to be put on the regular regime. Therefore he was first given Alevaire inhalation for five minutes at a time four times a day by direct application of the nebulizer to his

external nares. On the first day there was no change noted, so the treatments were prolonged to tolerance. At the end of the second day the patient coughed up a single large semi-solid mass of sputum which gave him instantaneous relief from much of his dyspnea. This was the first time in his life he had raised any sputum. At the end of the fourth day of treatment the patient coughed up an even larger and thicker mass of sputum. This mass was so large and solid that it traversed the larynx with difficulty and the patient could not get it all the way out of his throat for several minutes and this frightened him severely. Finally he was able to get it out, and he was then able to breathe easier than he had done for years. He would not take his treatment the next (fifth) day due to his scare, but on the sixth day he resumed the treatments. He raised small amounts of liquid sputum for the next four or five days, and finally was practically completely free of sputum. After the fourteenth day he was completely free of sputum and discontinued his treatments. He now goes outside, visits his friends, and does part of his own shopping. Although he still becomes dyspneic on prolonged exertion, he is no longer confined to his chair and his room, and he gives Alevaire full credit for his emancipation.

Case 11.—J. R. was a fifty-year-old colored male with severe chronic asthma characterized by a bronchospasm of remarkable degree and tenacity. He had been wheezing constantly in status asthmaticus for months at a time with no relief at all except when under heavy multiple medication. He had had few periods of freedom from wheezing during the entire twenty years of his illness and these periods were chiefly in mid-summer. He had no fever and a slight cough, rarely productive. The occasional plug expectorated did not afford much relief. The outstanding feature of his illness was not secretion but spasm. When he smelled any unusual odor such as fresh paint, or inhaled volatile or irritating materials, especially finger-nail polish and tobacco smoke, he developed an immediate exacerbation of wheezing. He had never smoked himself. Consulting dozens of doctors, including large clinics as well as "nature" healers, he had used many treatments and nostrums suggested for asthma. His daily medications for years included eight regular Tedral® tablets, two long lasting Tedral® tablets at bedtime, potassium iodide 80 grains daily, repeated whiffs of Vaponephrine® and Isuprel® during the day and an aminophylline suppository every night at bedtime. This routine gave him partial but not complete relief.

When the patient was started on Alevaire therapy it was felt best to treat him for long periods under a tent. However, the first night the patient stopped his treatment after about five minutes because he felt that the mist smothered him and made him worse. The next night his apprehension was calmed somewhat, and after repeated urging he consented to try again. He again felt a smothering and frightened sensation but stayed in the tent. After one hour he relaxed and began to breathe easier and he stayed in the tent the rest of the night. He was encouraged by the fact that he had awakened to cough and had taken medications less frequently than usual. Also he raised little sputum on arising, and wheezed slightly less than usual the next day. The third night the smothering sensation was absent, and he spent a better night than before. He continued sleeping in the tent, resting better each night and wheezing less each day, and on the eleventh day was completely free of wheeze all day for the first day in several years. He then reduced his treatments as instructed to one hour twice a day for fourteen days, during which time he was completely free of wheeze, and he had only a slight productive cough each morning. He then discontinued treatments entirely and remained symptom free except for the productive morning cough. As the weeks went by he found that "colds" and certain odors would still precipitate a wheeze. Then he would use Alevaire for thirty minutes at bedtime, and he would cough up some secretions and obtain relief. He stopped all

other medications except for an occasional whiff of Isuprel® at the onset of a cold or at the inhalation of an irritating odor. His outlook was tremendously improved, his sexual potency was increased and he was enabled to work with greater facility. Although he was apparently predominantly a "bronchospasm case" rather than a "secretion case," he still obtained marked relief with a prolonged treatment period.

Case 12.—W. M. H. was a sixty-year-old white woman with bilateral lower lobe bronchiectasis, nontoxic thyroid adenoma, rheumatoid arthritis and recurrent duodenal ulcers. Her chief difficulties were dyspnea and a scanty, thick mucopurulent expectoration.

Alevaire inhalation was given by direct application of the nebulizer to the nares for one hour twice a day using oxygen as the source of pressure. A rapid diminution in viscosity of the secretions and the expectoration of copious amounts of a thin liquid secretion followed. The patient experienced moderate relief in general, and became almost completely free of secretions. However, she felt that she was even more dyspneic after each treatment than before, and she discontinued them spontaneously. Her physician felt that the dyspnea after each treatment was due to a relative hyperventilation following the use of oxygen for an hour, and was in no way related to the Alevaire itself.

Case 13.—B. F., an eighty-year-old white man, had severe asthma with marked emphysema and pulmonary fibrosis. He turned on the compressor the first night and lay in the tent. However, he became aggravated by the noise of the compressor and by the necessity of being in a tent, and he discontinued his own therapy immediately.

Case 14.—J. H. M. was a sixty-four-year-old white man with severe asthma of fourteen years' duration. He had sought help from many physicians, and his last physician did a bronchogram and told him he had bronchiectasis as well as asthma. After repeated unsuccessful attempts at relief he became discouraged and quit going to doctors entirely. When he was finally brought in for Alevaire therapy, he was in severe status asthmaticus. His secretions were thick, mucopurulent and practically impossible to raise.

Alevaire was started in December, 1953, and the patient received one hour of direct nasal inhalation once a day in the physician's office. He improved rapidly, eliminated his secretions well, and by the seventh day there was practically no wheeze and relatively few rhonchi left. At the end of fourteen days of treatment he was completely asymptomatic and extremely pleased with his response. He was the only patient in this series who received antibiotics during Alevaire therapy, consisting of 1 cc of Combiotic® daily for ten days. This was given because of the presence of three plus neutrophils and many bacteria in his bronchial smear. This was not the definitive therapy, however, for he had received much heavier dosage of antibiotics many times before with little or no help. He has maintained his improvement and has had no exacerbations since cessation of Alevaire therapy.

Case 15.—W. M. was a thirty-four-year-old white male with chronic bronchial asthma of ten years' duration. He has had exacerbations on the average of every six weeks to three months all this time, and the attacks last an average of about five days. The attacks are moderately severe, with tremendous respiratory effort but no cyanosis. They continue through the nights, and reasonable amounts of sedatives and bronchodilator drugs give no relief and no sleep.

In December, 1953, he had a typical attack and was unable to sleep the first night. The next morning he came into his doctor's office and was given Alevaire inhalation for one hour. He stated that this relieved him "ten times better" than the usual bronchodilator treatment, and he slept well that night. He returned each day for five

days, receiving one hour's treatment each day. He breathed more easily each day, slept soundly every night without sedatives, and was completely free of wheeze when the course of treatment was completed. He has had no further difficulty and no attacks in the ensuing months.

Case 16.—B. L. was a sixty-eight-year-old white man with severe arteriosclerotic heart disease of four years' duration, and chronic auricular fibrillation. He also has chronic bronchial asthma and emphysema. He develops pulmonary edema and dyspnea at frequent intervals, and each attack requires hospitalization and intensive therapy, including prolonged residence in an oxygen tent.

In a recent attack, he did not respond well to oxygen therapy and was bothered a great deal by thick, copious bronchial secretions. These seemed to be a combination of edema fluid and mucopurulent secretions. He was given Alevaire inhalation by holding the nebulizer directly to his nose while in the oxygen tent. He was so weak that he was unable to hold the nebulizer for more than five minutes at a time, and it was necessary to have an orderly hold it for him. He was treated for one hour four times a day, and responded fairly well. The secretions became much thinner and were raised with much less difficulty. The chest became somewhat clearer, breathing was somewhat easier, and the aggravating cough was diminished. After the first few days he was strong enough to administer his own treatment without help. However, none of the symptoms were completely abolished, and edema fluid continued to form.

The use of Alevaire in this case was not as beneficial as in cases not complicated by cardiac decompensation. Yet it afforded definite increase in ease of expectoration and definite decrease in dyspnea. Even though the underlying cardiac disease was not improved, and edema fluid continued to form for two to three weeks, he was made more comfortable by being able to handle these fluids more easily. At the time of discharge, his secretions were thin and light, and were not troublesome.

Case 17.—C. S. was a sixty-one-year-old white man, with far-advanced pulmonary emphysema and fibrosis, a large fusiform aneurysm of the thoracic aorta, and chronic cor pulmonale. His condition dated back twenty-one years, when he had a severe case of influenza, followed by bronchopneumonia. Ever since that time he has had a severe cough, shortness of breath, and troublesome bronchial secretions. He has been confined to bed most of the time during the last seven years, and has been deteriorating rapidly in the last twelve months. Numerous hospitalizations have been necessary during this time, and an oxygen tank is kept beside his bed at home at all times.

In January, 1954, he was again hospitalized for treatment of pulmonary edema and dyspnea. He was digitalized rapidly and received relief from the pulmonary edema. However, the bronchial secretions were still troublesome, and caused some aggravation of the dyspnea, as well as an irritating cough. He was given Alevaire inhalation by direct application of the nebulizer to his external nares, for one hour twice a day. He also received postural drainage, expectorants, diuretics, and vitamins. He experienced definite increased ease of expectoration, raising his secretions with less difficulty, and by the fourth day of treatment, was nearly free of cough and was breathing much more easily. He was discharged from the hospital, and continued to use Alevaire at home, thirty to forty minutes daily, to prevent recurrence of mucous plugging.

This represents a case with multiple causes of cough and respiratory difficulties. The use of Alevaire was not expected to help any of the underlying diseases, but simply to eliminate the troublesome secretions. To this extent, Alevaire therapy was successful, as attested by the diminution in cough and dyspnea, and increased ease of expectoration.

COMMENT

The cases reported illustrate the marked mucolytic effect of Alevaire on retained secretions in the sinuses and bronchi. The degree of benefit was almost exactly correlated with the presence of thick, copious secretions or semi-solid mucus plugs. In practically every patient with retained secretions who underwent Alevaire therapy, these secretions were markedly thinned out and eliminated, with the result that the symptoms of cough, wheezing, dyspnea, and easy fatigability were greatly benefited.

The response in all such cases followed a definite, regular pattern, indicating a true specificity of effect. In the typical case, the secretions became thin and more easily expectorated after one or two days of therapy, and the elimination of secretions (and of symptoms) was completed within one to two weeks. Of course, the response is more rapid in hospitalized cases, who receive Alevaire for twenty-four hours each day, but this report concerns chiefly home and office treatments. Procedures and results of hospital therapy will be reported elsewhere.

In addition to the cases cited herein, the authors have had personal experience and received communications from other physicians concerning many other cases. There is a general feeling that the asthmatic patient with pure bronchospasm and no secretions sometimes responds to Alevaire, though not with the uniformity of cases in which secretions are present. Therefore, at this stage of our knowledge it seems that a trial of Alevaire is worth while even in patients with bronchospasm without apparent secretions. There is certainly some rationale in having such patients inhale a clean, filtered and intensely moistened air.

This does not pretend to be a controlled study. The patients happened to be the first known adults with these diseases treated with Alevaire in Mobile, Alabama by their private physicians. They were simply collected into this paper and reported so that the profession as a whole, and research centers in particular, could initiate large scale controlled studies and possibly extend the apparent benefits of Alevaire to a larger number of patients.

All these patients had a routine history, physical examination, x-ray and indicated laboratory studies, but none were skin tested or otherwise investigated from an allergy standpoint. No vital capacity tests were made, although this procedure will be included in future studies. Most cases received no other medication than the Alevaire itself, and in fact most were taken off of previously prescribed medications. We emphasize that this was done only for study purposes, and that we do not claim that Alevaire alone is all that is needed for all cases. Now that we have satisfied ourselves with the value of Alevaire, we have integrated it with our overall care and total management of respiratory diseases, including complete etiologic workup, and employing all medications at our disposal. This preliminary report is not an attempt to draw final conclusions or make sweeping claims but is simply an effort to stimulate further study.

SUMMARY

A new mucolytic aerosol solution, Alevaire, heretofore used successfully in infants and children for the treatment of bronchial obstruction due to thickened secretions, has now been applied to adult patients.

The treatment of sinusitis, bronchitis, bronchiectasis and bronchial asthma with this special aerosol by inhalation is described. Alevaire proved very effective in dissolving and facilitating the elimination of retained secretions in the sinuses and bronchi. In almost every case the degree of relief was correlated with the presence and thickness of retained secretions. Thick, yellow, solid sputum which had been expectorated with difficulty became thin, colorless and liquid sputum which was expectorated with ease and gradually diminished in volume. Labored breathing and insomnia, which previously had necessitated orthopneic sleeping positions and the almost daily use of sedatives, soon were replaced by easy respiration and ability to enjoy normal restful sleep. The habitual use of other medications soon became unnecessary. Occasionally a mild sinusitis was successfully treated with only a nose drop mixture containing equal parts of 1 per cent Neo-synephrine® and Alevaire.

The two techniques of Alevaire aerosol inhalation employed in this study are (1) the open-top tent method of overnight therapy and (2) the direct application of a nebulizer equipped with a nasal tip to the external nares for short periods of therapy.

A preliminary report of seventeen case histories of adults treated with this specific aerosol is presented.

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AIR POLLUTION CONTROL ASSOCIATION

The Air Pollution Control Association will hold its first semi-annual technical conference in the Biltmore Hotel in Los Angeles, California, November 4-6, 1954. The aim of this national society is to make possible a pooling of knowledge from industry, science, and government which will aid in bringing about the most effective control of atmospheric pollution with the minimum cost. The Los Angeles area was chosen as the site of this conference in recognition of the vast amount of knowledge which has been gained there from research and control activities. The association has arranged this meeting to enable participants to learn first hand of the most recent developments in the various fields of air pollution control. The

SOME OTOLARYNGOLOGIC PROCEDURES USEFUL IN TREATING THE ALLERGIC PATIENT

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OTOLARYNGOLOGY was already a well-established specialty at the dawn of the allergic age. Learning quickly that about 70 per cent of chronic nasal complaints and about 90 per cent of chronic sinus conditions have some basis in allergy, many otolaryngologists incorporated allergic management into their therapeutic armamentaria. Naturally, this integration necessitated changes in otolaryngologic practice. Some procedures, e.g., sinus surgery, are indicated less frequently. However, it was often found that the results of allergic management could be enhanced by the simultaneous application of some of the time-honored and proved methods of this specialty.

A large percentage of the practice of the general allergist is devoted to the treatment of respiratory tract allergy. This presentation will discuss some of the procedures which we have found to be of value in our practice of otolaryngologic allergy.

THE USE OF NOSE DROPS

A large segment of otolaryngologic opinion today flatly condemns the use of nose drops in any patient, advising the use of oral vasoconstrictors instead. While the objections to topical vasoconstriction are well taken, in our experience the vasoconstriction, ventilation, and drainage provided by properly-used nose drops is superior to that obtained with oral medications. Further, we feel that nose drops are not harmful if used in the proper amount and concentration and for not too prolonged a period of time. They should never be used more than four times daily for three days.

Generally speaking, we advise patients with all types of nasal allergy against the use of nose drops. However, if there is superimposed infection of the nose, nasopharynx, sinuses, or a complicating secretory, catarrhal, or purulent otitis media, we do not hestitate to prescribe nose drops in order to promote ventilation and drainage. In these instances, our personal preference is 0.5 per cent Neo-synephrine® since it meets most of the criteria for a good topical vasoconstrictor. Nose drops containing antibiotics, sulfonamides, antihistaminics, etc., are not used because we feel that if these medications are indicated, it is more rational to administer them systemically.

If nose drops are prescribed, the patient is directed to use them four

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times daily in the Parkinson position. This is done because the drops are thereby brought in contact with all of the important structures on the lateral wall of the nose. Each patient is given printed instructions which detail the position of the patient, the amount of solution and the duration of application; these are available at low cost from large medical printing firms or may be mimeographed. It is our strong conviction that every physician prescribing nose drops has a moral obligation to instruct the patient to use them properly; otherwise he is wasting both the patient's time and money.

When allergic control has not been achieved in uncomplicated cases of nasal allergy or seasonal hay fever, and the patient cannot, or will not, tolerate his symptoms until it is, we have used the following prescription to excellent advantage:

RX: Propadrine® .....gr 3/8
Pyribenzamine® .....gr 3/8
Seconal® .....gr 1/4
Atropine .....gr 1/200
M. & ft. 20 such caps.
Sig: One q. 4 to 6 hrs. only prn for severe allergic symptoms.
(Do not refill)

This formula is designed for vasoconstrictor, antihistaminic and parasympathetic blocking action; the barbiturate is incorporated to give some central sedation and thereby counteract the stimulating action of the vasoconstrictor. In addition to using this prescription for seasonal hay fever we have also found it effective in acute exacerbations of perennial nasal allergy and in the treatment of rhinitis medicamentosa.

ERADICATION OF SINUS INFECTION

Chronic infection of the paranasal sinuses often accompanies or complicates respiratory allergy. The frequent occurrence of chronic purulent sinusitis with bronchial asthma, so-called asthmatic bronchitis in children, and allergic cough are cases in point. Of all the sinuses the ethmoids are probably the most commonly overlooked offenders. Spectacular improvement often results from the eradication of these infections.

It should be emphasized here that the classic signs of acute sinusitis are rarely seen and the patient's complaints referable to the sinuses may be minimal. Discovery of the offending locus is usually the result of finding gross mucopus about the ostia of the sinuses or along the nasal pathway, increased density on x-ray examination, or as a result of a diagnostic lavage. It is this latter procedure we should like to discuss briefly.

Sinus lavage may be accomplished in one of three ways: by puncture of the bony wall or membranous septum separating the nasal passages and sinuses, by canulation of the natural ostia of the larger sinuses, or by displacement. We use the latter two methods most frequently for treat-

ment and diagnosis; of these, canulation of the natural ostia requires special skill, but displacement, particularly for diagnostic purposes, does not.

This useful diagnostic tool may be used if ethmoid infection is suspected

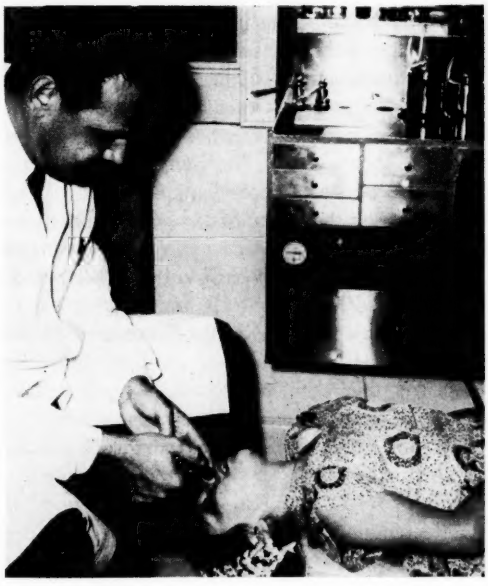

Fig. 1. The position of the patient during displacement. The patient is an eight-year-old child.

in spite of negative x-ray reports, or if infection is known definitely to be localized in the ethmoids.

Displacement was first devised by Proetz,[4] the great nasal physiologist, and the procedure bears his name. He reasoned that if negative pressure is applied to the orifice of a container whose walls are rigid (e.g., a sinus), part of the contained air will be sucked out and will rush back in when the negative pressure is released. Since the sinuses empty into the nasal cavity, and since the soft palate can be used to close off one end of the cavity by phonation, negative pressure applied to the nostril will cause exchange of air between the sinuses and the nose in the same manner as if it were applied directly to the ostia. Now if the ostia of the sinuses are covered with fluid, e.g., normal saline or a mild vasoconstricting agent, two things occur when the intermittent suction is applied to one nostril while the other is being occluded and the patient phonates: (1) pus, or other secretions blocking the ostia, will be evacuated, and (2) the normal saline

or vasoconstricting agent will rush into the sinuses when the negative pressure is released.

In practice, after the patient's nasal membranes have been shrunken by the use of a vasoconstrictor applied by atomizer or drops in the Parkinson position, he is placed on his back on a chair, couch or treatment table. His head hangs over the end of the table in hypertension, the external auditory meatus and the chin being in the same vertical plane. The nasal cavities are then filled with a warmed 0.25 per cent ephedrine solution and he is directed to continuously repeat the word "kay" in order to close off the nasal cavity with the soft palate. Gentle, intermittent suction, never exceeding 5 to 8 mm of water, is applied to one nostril while the other is compressed with the finger. Any muco-purulent material in the ethmoids will be replaced by the ephedrine solution which exerts a continued shrinking action on the lining of the cells and their ostia long after termination of the procedure. At times this purulent material will often be obtained in the form of what appears to be almost perfect casts of the sinuses and is ideal to culture when an autogenous vaccine is to be made. Figure 1 is a representation of the displacement method being used on a child eight years of age.

For therapy we use this method every three or four days for three or four treatments. If no improvement is noted, the treatment is abandoned. When used for treatment, it should not be the only therapeutic measure employed.

As an addendum, it might be mentioned that it is possible to introduce contrast media into the sinuses by this method in order to delineate their contour.

NASAL CYTOLOGY AND POST-NASAL DISCHARGE

At first glance, it would seem trite to discuss cytologic study of nasal mucus before a group of allergists. However, we otolaryngologists frequently see a condition in allergic and other patients which might be confused with post-nasal discharge due to allergy, and cytologic examination is a very helpful differentiating measure which can be employed.

Individuals complain of a nonpurulent post-nasal discharge either (1) when the amount of mucus is profuse, as in allergic rhinitis, or (2) when the mucus is thick and does not move normally along the path from the nasopharynx, down past the pharynx to be swallowed. In the latter instance, the patient becomes conscious of the thickened mucus and begins to make strenuous efforts to remove it. Sometimes an actual fixation develops and efforts to obtain relief, particularly on arising in the morning, become persistent and often violent, and actually lead to nausea and vomiting. Patients with this condition complain of a seeming paradox, i.e., they say they have a post-nasal discharge and yet complain of dryness of the mouth and throat.

Viscosity of mucus depends to a large extent upon the vascular supply

of the region producing the mucus and the state of the secretomotor system supplying the glands. When it becomes too viscid it will roll over in masses. It is at this point that the patient becomes conscious of it and symptoms begin.

This condition is frequently seen among those who use antihistaminic drugs. Apparently the action of the drugs leaves the action of adrenaline unopposed and the vasoconstriction thereby produced causes increased viscosity of the mucus and the sensation of dryness in the mouth and throat. It also frequently occurs after infections, when the patient is exposed to dry heat, and when tension states exist.

If a cytological examination of the nasal secretions is done, much mucus with very few cells will be found.

Treatment consists of stopping the antihistaminic drug and substituting another less powerful for the particular patient, or employing a sympathetic blocking agent. We have used a sublingual preparation of dihydrogenated ergot alkaloids called Hydergine® to great advantage; in some cases we have combined this preparation with oral prostigmin bromide to reinforce the action of the Hydergine.® Our rationale is to block the sympathetic nerve supply and thereby leave the parasympathetic secretory system unopposed, and secondly, to improve blood supply as a result of vasodilatation and thus re-establish normal viscosity. Our object is not to "cure" or abolish the post-nasal discharge; rather it is to re-establish the normal mucous pattern.

BRONCHOSCOPY IN THE TREATMENT OF ASTHMA

Despite the fact that many articles in the literature attest to the value of bronchoscopy in the management of patients with respiratory allergy, it is our opinion that the procedure is still virtually neglected. We feel this is unfortunate, because bronchoscopy can prove of value to the allergist in many ways.

Undoubtedly it is most dramatic in the treatment of status asthmaticus; in this condition it is not unusual for the patient to feel better immediately and for his respiratory efforts to be visibly lessened as soon as the heavy mucoid secretions are removed by suction. Sometimes the cycle is broken by bronchoscopic aspiration, but the reason for this is not clear. We are aware of the argument that during bronchoscopy it is not possible to suction far enough along the smaller bronchioles of the tracheobronchial tree to be of any real benefit. However, the proof of the benefit obtained is found in the subjective and objective improvement that ensues.

Bronchoscopy may also be used to advantage by the allergist in differential diagnosis. Chevalier Jackson's famous dictum still holds: "All that wheezes is not asthma." Too, it is valuable for discovering the presence of complicating bronchiectasis either by direct inspection or by serving as a means for the instillation of contrast media.

The technique of bronschoscopy may be found in any standard textbook.

We will mention only a few points which should be taken into consideration when submitting allergic patients to bronchoscopy. To keep trauma at a minimum we feel the procedure is best done under local anesthesia. When the patient is in status asthmaticus, the topical anesthetic may be injected into the trachea directly through the cricothyroid membrane, or the procedure may be done with no anesthesia whatsoever. In patients other than in status, three grains of Seconal® are given two hours before introducing the bronchoscope; this is followed by 100 milligrams of Demerol® and 2 grams of mephenesin, a skeletal muscle relaxant, approximately forty-five minutes before the procedure is started. We never administer atropine or morphine to our allergic patients and advise the administration of intravenous aminophylline a short time before in order to obtain some degree of bronchodilatation. It is well to insufflate oxygen through the bronchoscope during the procedure.

With a full realization that we may be thought radical, it seems to us that part of the training of the allergist should be in bronchoscopy. He is, in a sense, as much a "chest physician" as is the thoracic surgeon or the phthisiologist and has the right and obligation to avail himself of every diagnostic and therapeutic measure at his command for the proper management of his patient.

HEARING LOSS IN ALLERGIC CHILDREN

The role of allergy in the production of hearing loss and other ear disorders in children has not received the attention it deserves. As authority for this statement, we report the results of a recently completed hearing survey, directed by Dr. Rubin, of 6,000 children in the first grades of the parochial schools of the city of New Orleans. As expected, most of the hearing difficulty encountered was of the conductive type. Surprising, however, was the finding that about 75 per cent of these children had nasal allergy which played the major part in the production of the difficulty.

These observations have confirmed clinical impressions formed over the years. In the otologic examination of allergic children, one frequently finds a secretory otitis media which has produced no symptoms of which the child complains or the parents are aware. The average parent is both surprised and concerned to learn that the ears are involved and, perhaps, that there is some hearing loss. Of course, there are cases which have symptoms consisting of one or more of the following: intermittent hearing loss, recurring ear pain, frequent abscess formation, and chronic drainage from the ear. Because we speak as a result of hearing, the loss may be first suspected when the child does not speak correctly.

Allergy affects hearing, in most instances, because it interferes with proper functioning of the Eustachian tubes either directly or indirectly. At times allergic edema of the walls of the tube is at fault. Most frequently, however, allergy causes proliferation of the nasopharyngeal lymphoid elements which occlude the ostium of the tube. In either case, air con-

tained within the middle ear is gradually absorbed by the blood stream, the tympanic membrane cannot move properly, and hearing loss ensues. In some instances, there is an outpouring of a serous exudate into the middle ear; this may or may not cause hearing loss immediately but is always potentially dangerous because, should organization of this material occur, the result may be the production of chronic adhesive otitis media which causes an irreversible type of conductive hearing loss.

Proper management of these cases does not always consist solely of allergic therapy. In addition, measures should be taken to relieve the Eustachian tube obstruction until control of the allergy is accomplished. Otologic opinion should be sought regarding the advisability of removing any serous exudate from the middle ear and/or eliminating the nasopharyngeal obstruction by surgery, x-ray, or radium therapy.

Because of the importance of hearing in the physical, mental and behavioral development of the child, we feel that the allergist should be very cognizant of the possibility of hearing loss in children with respiratory allergy. The best course to follow would be to learn to recognize the presence of retracted tympanic membranes, blocked Eustachian tubes, and secretory otitis media. The only way this can be done is by making an otoscopic examination part of the work-up of every allergy patient.

MODERN NASAL SURGERY AND THE ALLERGIC NOSE

Much has been written concerning the performance of surgery in the allergic nose; therefore, it occurred to us that a discussion of the latest developments in the field of rhinologic surgery might prove of interest. Further, we thought that the allergist might like to learn the well-considered conclusions reached in the light of these developments by some of those who do both otolaryngology and allergy.

Before the advent of the sulfonamides and the antibiotics and the realization of the importance of allergy in the production of many nasal disorders, the destructiveness of nasal surgery, although undoubtedly warranted in many instances, often so disturbed nasal physiology that the patient became a nasal cripple forever thereafter. To be fair it must be admitted that the rhinologist of that bygone era worked without the advantage of the modern antibacterial agents and the knowledge of allergic diagnosis and management. He was entirely on the defensive in that the only weapon he possessed was the ability to eradicate tissue wherein the ravages of allergy with superimposed infection had already taken their toll; he was in the same situation in which the modern surgeon combatting cancer finds himself—he must excise the lesion, and, in so doing, often must sacrifice so much tissue that the physiology of the organ is seriously disturbed or, in some instances, destroyed.

The modern rhinologist possesses powerful chemotherapeutic agents, the ability to correct, or have corrected, coexisting allergic, metabolic and psychosomatic disturbances, and has the most advanced surgical techniques

at his disposal. Yet, over the years, the otolaryngologist has witnessed failure of even the most adequately performed intranasal surgery and the most cosmetically-satisfying external nasal procedures because of failure to correct allergic, metabolic, and psychosomatic disorders. On the other

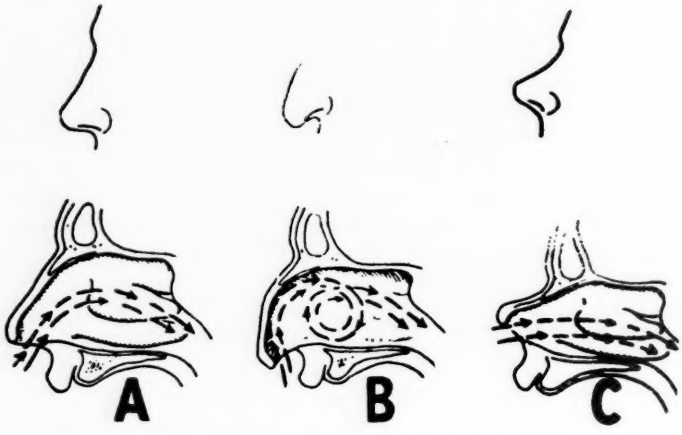

Fig. 2. (A) Pathway of air stream in a normal nose. (B) Effect of a depressed tip and dorsal hump on the nasal air stream. (C) The air stream in a nose whose tip is unduly elevated.

hand, he has seen individuals in whom these latter factors had been controlled fail to obtain complete relief because of the presence of some anatomic abnormality which disturbed nasal physiology. He has been forced to conclude that his therapy must be directed against all the factors which interfere with the re-establishment of nasal homeostasis; failure to do so will lead to disappointing results.

Here, then, is the crux of the problem of surgery in the allergic nose. Allergy is but one disorder which may interfere with proper nasal function and so may often occur in combination with others. To do complete justice to the patient, all etiologic factors must be traced down and attacked. As each disturbance is corrected, management of the remaining ones becomes less difficult and the part played by them in the overall picture easier to define.

Though some of the old surgical techniques are still used, many have been modified and new ones have been devised. These new procedures are based on sound physiologic principles and have as their object either the preservation or restoration of nasal function. A discussion of the thinking underlying modern nasal surgery seems timely.

Proetz[4] has long since pointed out that to function properly the nasal passages must present a "streamlined" configuration to the passage of in-

spired and expired air. Streamlining is dependent, among other things, on the size, shape, and direction of the external nares and nasal pyramid, the configuration of the internal nasal chamber, and the relative sizes of the anterior and posterior nares. Abnormalities in these regions

Fig. 3. A thirty-seven-year-old patient with nasal complaints, headache and conductive hearing loss due to a combination of the effects of allergy and structural abnormalities of the internal and external nose. (Left) Patient is shown before combined external and internal nasal surgery. (Right) Postoperative view.

result in the production of unnatural turbulence or eddies in the inspiratory or expiratory air currents (Fig. 2) and cause local drying of the mucous membrane, interference with ciliary action, increased viscosity of the nasal mucus and increased precipitation of particles, including bacteria, viruses, and allergens, from the inspired air.

We have slightly modified Boies'[2] division of the causes of nasal obstruction into three groups:

I. Extranasal defects involving:
   A. The nasal bones (depressed fractures, humps, lateral deviations, narrow bridge, and so forth.)
   B. The cartilage
      1. The upper laterals (the so-called respiratory valve.)
      2. The lower laterals.
   C. The anterior nares (depressed or elevated tip, large alae, collapsed alae, columella abnormalities.)

II. Intranasal defects involving:
   A. The septum (deviations, impactions, dislocations, spurs, fractures, etc.)
   B. The lateral nasal walls (chronic allergic and non-allergic rhinitis, metabolic and psychosomatic disturbances, new growths, etc.)
   C. The posterior nares (choanal atresia, polyps, etc.)

III. Nasopharyngeal defects (hypertrophied lymphoid elements and new growths.)

An example of a case in which both allergy and structural abnormalities were operative in the production of symptoms is seen in Figure 3. This thirty-seven-year-old woman complained of moderate nasal blockage,

headache, intermittent attacks of left ear pain, some loss of hearing in the left ear, and postnasal discharge. A nasal smear revealed the presence of a diagnostic eosinophilia. Intradermal skin tests were positive to house dust, a mixture of atmospheric molds common in this area, and tobacco smoke. Otologic examination revealed the presence of a conductive hearing loss in the left ear as a result of left Eustachian tube blockage. Rhinologic examination demonstrated the obvious external deformity but also spurring and deviation of the septum to the left. Hyposensitization and elimination measures were instituted and when improvement to the extent considered maximal for this type of therapy was obtained, the external nasal and septal deformities were corrected. Her symptoms cleared completely and, though her nose still blocks on massive exposure to the above named allergens, she seems to be able to tolerate normal exposure and does not deem continued allergic management necessary.

It might be mentioned that we have observed this latter phenomenon in a number of cases. Following re-establishment of the normal air pattern there seems to be a heightening of the threshold of symptoms so that the patient is apparently better able to tolerate exposure to previously offending allergens.

The story of modern, physiologic nasal surgery is so fascinating that we are certain every allergist or other physician who deals with alterations in respiratory and circulatory dynamics would be interested in some of the more complete writings on the subject. One which we can highly recommend is a recent article by Fomon, et al.,[3] in which the role played by the nose in regulating intrathoracic, sinus, and middle ear pressures is reviewed, the manner in which the nose prevents hyperventilation or hypoventilation is demonstrated, the effect of nasal stenosis (from various common causes) on lung ventilation and air mixing is shown, and the aid given by the nose to the cardiovascular system is elaborated.

ACKNOWLEDGMENT

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INTRANASAL EXAMINATION AND TREATMENT OF THE ALLERGIC NOSE

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ON the practical side of ear, nose, and throat examination and treatment of the allergic patient, I feel that anything which disturbs the normal physiology of the nose will be followed by compensatory reactions of the mucous membrane of the nasal meatuses and sinuses. It is not difficult to shrink the nasal tissues with a number of astringents, but all shrinkage is followed by a compensatory swelling, which is most uncomfortable. This prompts the patient to use more medication, which in turn is followed by a similar swelling, until the tissues become so waterlogged and edematous that they fail to respond to artificial stimulation. Every available millimeter of space is occupied by edematous tissue until the original drops or astringent will not even enter the nose. The patient is not only uncomfortable from his original allergic rhinitis, but also from the allergic response to the introduced chemical, the increased nervous reaction, and lack of sleep from the systemic absorption of the material. My own personal opinion is that the less material an allergic individual puts into his nose the better he will be.

Very often a patient comes to the office with a badly blocked nose and, upon questioning, will give a history of constant blockage the year round, usually worse in the winter. When asked about previous treatment, we find that he has usually had a course, possibly a year or more, of vaccine therapy from one or more allergists and has lost faith in the use of vaccines—and justly so, for on careful examination we often find the posterior half of the nasal passages almost completely blocked by a badly deviated nasal septum. Often there are sharp spurs or ridges on either side of the septum. Sometimes the septum makes contact with the turbinates on both sides. Even synechia or adhesions may bind the turbinates to the deviated septum. Of course, no amount of vaccine therapy is going to make these individuals comfortable. Their noses are mechanically blocked, and the bony obstruction of hard tissue must be removed before the remaining allergic or edematous swelling can be reduced by medication or desensitization. A blocked nose is always sensitive to dust, pollen, or other irritants, while a nose that is well-drained and ventilated tends to rid itself of waste products and become healthy. These patients are often the unfortunate victims of the patent medicine man and, as a rule, have used almost every form of nose drops advertised by radio, TV, magazines, or newspapers.

In making nasal examinations, learn to use your nose speculum. If you cannot get accustomed to a head mirror, get one of the headlight variety

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and learn to use it. Do not look just within the nasal vestibule and call the nose negative. The obstruction is rarely there, unless traumatic. Look further back, shrink the tissues with a weak cocaine or antipyrin solution or any weak astringent. Examine carefully the inferior and middle meatuses. One should be able to see the posterior wall of the nasopharynx or the adenoid region glistening through. One should be able to pass a moistened cotton-tipped metal applicator through to the posterior pharyngeal wall, or else there is some obstruction present. Don't attempt to use a wooden stick, as these break off easily and are difficult to remove. Always tell the patient after such an examination with shrinkage that it may be followed by compensatory swelling similar to the type which develops after using proprietary nose drops; otherwise, he will think he is worse after his very first visit to you. If there is obstruction, such as a deviated or very much thickened nasal septum which must be removed surgically, make an effort to determine the nature of it. Often you will find a swollen beefy middle turbinate which has undergone polypoid degeneration. Many times the turbinate, instead of being the size of the tip of a nasal speculum, is enlarged to the size of the thumb, with numerous polypi extending from the pendulous or inferior surface. Such tissue is pathologically beyond recall with a vaccine, cortisone, et cetera, and must be cleanly removed. As a rule the snare does a good clean job if the involved turbinate is fractured over toward the midline and the snare loop is shoved over it and tightened until it cuts off clean at its attachment to the lateral bony wall. Frequently this brings into view innumerable polypi protruding from the ethmoidal labyrinth. Often with the relief of pressure these polypi or polypoid buds can be seen mushrooming out from the ethmoidal area, which requires exenteration or a thorough cleaning out of that region down to the orbital plate. I realize that few allergists do that type of work, but it does point out the need of cooperation between the allergist and the otolaryngologist. Likewise, no otolaryngologist is going to be a good specialist unless he cooperates with the allergist. Let me emphasize that my last statements have been with the middle turbinate in mind. We do not remove the inferior turbinate in allergic conditions, although this may be done in case of malignancy.

The inferior turbinate, as you know, is needed to warm and moisten air to the lungs, and its absence would cause a constant dry throat and irritating cough. The inferior turbinate does not become cystic or polypoid as often as does the middle turbinate, which is constantly bathed and irritated by purulent secretions from the ethmoidal or cold cells. If the other parts of the nose are put in good condition the inferior turbinate responds well to the live cautery, to electrocoagulation, or to electrodesiccation. With the live cautery the turbinates are deadened with a solution of cocaine or with whatever local anesthetic material is preferred. The patient takes a big breath and then blows it out slowly through the nose, as a cautery streak is made along the median or inferior surface, or both, from the an-

terior tip to the posterior end. The reason for the big breath before commencing cauterization is to prevent the patient from breathing in a chest full of smoke from the frying tissue, which, as you know, is not pleasant. The cautery line is made as the patient exhales. This cautery line may be repeated two or three times at one sitting without pain. In electrocoagulation and electrodesiccation the method is essentially the same except that a different type electrode is used. A short while after this procedure the tissues swell, the nose becomes blocked for about forty-eight hours and runs as though from a fresh cold, then healing and shrinkage set in and the nose begins to open. In about two weeks the swelling is completely reduced and the patient's breathing is markedly improved. Occasionally we are forced to take off the anterior tip of the interior turbinate, and very often the posterior tip, which has a habit of becoming polypoid and enlarged, but never the entire inferior turbinate.

Here again let me emphasize the importance of a thorough nasal examination. No examination is complete unless we examine the nasopharynx, the nasal "blind spot." The examination of the postnasal space is not easy on some patients on the first visit. It is often difficult for them to breathe through the nose with the mouth open, so I don't stress it too much at first. I instruct them to get before a mirror at home and breathe until they can breathe through the nose with the mouth open. When the palate relaxes, assumes its normal resting position, and a postnasal mirror can be inserted beneath it and the posterior choanae inspected, often a bursa or enormous polypoid posterior tip of the inferior turbinate can be seen and removed through the nose. At other times we use the nasopharyngoscope, which is inserted through the nose like a minute periscope and turned at any direction, affording a good examination of the posterior nasopharynx. A pontocaine spray is useful, but the patient must be cautioned to spit it out and never use it as a gargle.

Before we leave the nasal cavities let me say a word more about polypi. I feel there is no substitute for complete surgical removal down to the last vestige of the attachment or root, even if an ethmoidectomy has to be done. Allergic treatments may then follow. I have occasionally heard the statement made that the larger portion of the polyp should be removed and the stumps would disappear under allergic treatment. Unfortunately that has not been my observation in the cases I have had the opportunity to observe. Neither have I seen many that I could feel had disappeared with the use of cortisone and allied compounds; however, I feel that the use of radium, as a rule 100 mg capsules, inserted into the nose for a varying length of time, has given excellent results in preventing recurrence of polypoid growth where the growth and all visible roots have been removed. Some of these cases have stayed free of return of polypi for many years.

If one would but look into a badly involved maxillary sinus at the time of the Caldwell-Luc or radical antrum, where we go into the sinus under the cheek, and see the tremendous number of polypi and enormously

thickened membrances, the entire nose bathed with purulent material, we would realize what a tremendous job we are giving vaccines to do. The old dictum which was true two thousand years ago is still as true today—"Ubi Pus, Ibi Evacuae" ("Where there is pus, get it out."), whether it is allergic pus or pyogenic material.

Another aid in examining the sinuses is the use of a transilluminator, a simple electric light and a rheostat for comparing size and clarity of the maxillary sinuses and the frontals. If in doubt, a small cannula can be inserted through the natural ostium of the antrum and the sinus irrigated with a saline solution in a few moments. The irrigation of an antrum does not necessarily call for a puncture of the antrum, which causes some patients to shudder at the thought. It should be done without pain or bleeding. I can see no use for displacement, tampons, or packs in the treatment of allergic conditions, no matter how much I might value these methods for pyogenic or purulent infections. I feel towards displacement treatment in allergy as I do towards proprietary drops that too much treatment is bad for the patient.

It is not always easy for the roentgenologist to differentiate between a pyogenic process and allergic swelling. But as a rule in an acute infectional sinusitis x-ray shows a faint haziness of the mucous membrane, with a faint rim of thickened mucosa around the periphery of the sinus. In an allergic condition we usually have a greater thickening of the mucous membrane with a bulging toward the cavity and swollen turbinates; in both types the bony wall is intact. If the allergic swelling persists we may have sufficient increased density to simulate a chronic sinusitis in two or three days, and we get a picture of homogenous clouding of moderate density.

The real problem of the otolaryngologist the last few years has been secretory otitis media, the collection of fluid, exudate or transudate, within the eustachian tube or middle ear. The diagnosis is usually made on the patient's complaint, sometimes it can be verified by the appearance of the ear drum, but it usually requires the use of an eustachian catheter and compressed air. If compressed air is available, don't rely on the Politzer bag. When a small current of air is blown through the eustachian tube, a crackling or rales may be heard. Paracentesis or repeated drainage so far has given relief, but many investigators believe that allergy is the underlying factor for this annoying condition. I do hope that some day the allergist can come to our rescue.

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A NEW TUBERCULIN TEST WHICH DETERMINES THE AMOUNT OF ALLERGY AND IMMUNITY TO THE DISEASE

(Abstract)

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A PRELIMINARY and short report on a new tuberculin test developed by Dr. Jose M. M. Fernandez (Argentina) is presented. The test is analagous to the lepromin test.

In the lepromin test, specially prepared tissue from nodules of lepromatous leprosy (containing M. leprae) is injected intradermally and the test is read in forty-eight hours and in three weeks. Extensive research work has shown that the forty-eight-hour reaction (Fernandez test) is indicative of the allergic response of the individual to the *M. leprae* bacillus and the three weeks' reaction (Mitsuda test) is indicative of the immunity that a person has to leprosy. The lepromin test helps simplify the classification of leprosy and, depending on its intensity, prognosis can generally be given, i. e., markedly positive lepromin reactions are found in cases of tuberculoid leprosy (which generally is a self-limited disease which some authorities feel requires no treatment in most cases). Contrariwise, lepromatous leprosy gives negative lepromin reactions (and generally has a serious prognosis unless treated).

In this new tuberculin test, all the elements present in the tuberculosis bacillus and its capsule are injected intradermally and, like the lepromin test, it is read in forty-eight hours and in three weeks. The significance of the two reactions is similar to the lepromin reactions. The forty-eight hour-reaction denotes the allergic response to tuberculosis infection while the three-week reaction is indicative of immunity to the disease.

It is beyond the scope of this paper to explain cross sensitization and immunity existing between leprosy and tuberculosis, and its effects on the tuberculin and lepromin tests.

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PROPER USE OF AEROSOL TRYPSIN IN BRONCHIAL ASTHMA AND OTHER CHEST DISEASES

(Abstract)

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TRYPSIN HAS been proven, by laboratory methods and clinical trials, to be a safe and effective mucolytic agent. Clinical use has shown that aerosol trypsin causes bronchial flushing, thinning of sputum and temporary increase of coughing, followed by decreased expectoration and cough when the air passages are cleared out. Side effects are few, if proper technique is carefully observed. Especially important are the use of epinephrine and antihistaminics prior to treatment and washing out of the nose and throat afterwards.

Because of its mucolytic powers, trypsin theoretically should be very beneficial to asthmatic patients. However, our trials with eighty-one patients proved very disappointing. Only five of thirty-three patients with chronic bronchial asthma and emphysema showed good results, while eighteen were classified as treatment failures. Results were much better in a group of paroxysmal asthmatics; the group was, however, too small for any valid conclusions.

The main use of aerosol trypsin appears to be in the treatment of bronchitis, bronchiectasis and atelectasis. Our own patients showed excellent or good relief in all but two of forty patients in these categories. It was especially helpful in bronchial asthma accompanied or complicated by infectious bronchitis or pneumonitis.

Because of these results, it is theorized that aerosol trypsin should prove of great benefit in preventing the occurrence of bronchial abnormalities which sometimes follow various types of pneumonia, particularly primary atypical pneumonia. Morle and Robertson in England, and Bachman et al in the United States, have shown conclusively that these pneumonias are accompanied by a high incidence of bronchial abnormalities (shown by bronchograms on soldiers with pneumonia). In almost all cases, these changes were reversible. It is probable that even the small percentage of permanent abnormalities can lead to a rather large number of cases of bronchiectasis, since primary atypical pneumonia is treated very casually nowadays; the patients are rarely followed closely.

In particular, Morle and Robertson separated out a new type of pneumonia, which has previously been included in the group of primary atypical pneumonia. This new type, called "segmental aspiration pneumonia" is

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Presented at the Fifteenth Annual Meeting of the Southwest Allergy Forum, New Orleans, May 10, 1954, prior to active duty in the Army.

Dr. Unger is Instructor in Medicine, Allergy Clinic, Northwestern University Medical School, Chicago, Illinois; now in active service with the U. S. Army at El Paso, Texas.

characterized clinically by the onset of hacking cough following a U.R.I., accompanied by initial fever, which quickly subsided. X-rays show a triangular patch of pneumonitis, often seen only on lateral films. The patients do not respond to antibiotics, but react better to postural drainage.

Trypsin should prove of great benefit in this group of patients. Our experience has been uniformly excellent with all patients (approximately fifteen now) responding completely to two to four treatments. Further trial with this group is urged.

William Beaumont Army Hospital
Box 137, El Paso

INHALANT FACTORS IN ATOPIC ALLERGY

Every case of atopic allergy should receive immediate attention regarding avoidance or elimination measures, whether the patient is treated in the hospital or in the home. Although food allergy may be of importance at the onset of treatment, the inhalant factors are considered by far the major factor which must be controlled as much as possible. An environment low in common inhalant offenders must parallel immunization procedures for the most beneficial results.

One of the most practical methods is the prevention of the patient from contacting inhalant allergens, such as dust, molds, pollens, et cetera. Allergen-free or allergen-proof bedding and furniture, dust sealers, and air filters are available and reasonably priced, and should be considered as requisites to insure the maximum results when applying other management procedures.

DIESEL ENGINE DERMATITIS CONTROL

Since the advent of the diesel locomotive, the railroad industry has noted a marked increase in the number of cases of occupational dermatitis. This has been the result of the extensive dieselization program which the railroads carried on during and immediately following World War II, according to Robert Plunkett of the Great Northern Railway, St. Paul, Minnesota, as recorded in *Minnesota Medicine* for May, 1954. The occupational dermatitis is due to the tremendous increase in the use of petroleum products and derivatives essential to the operation and maintenance of diesel locomotives.

ANTIBIOTICS IN THE ALLERGIC PATIENT

(Abstract)

EDWIN D. KILBOURNE, M.D.
New Orleans, Louisiana

The use of antibiotics in the allergic patient constitutes a therapeutic dilemma. While the need for antimicrobial therapy of secondary skin and respiratory tract infections is increased, so is the hazard of drug hypersensitivity. The exact nature and magnitude of the problem of antibiotic hypersensitivity have not been defined adequately. Few studies have attempted to distinguish hypersensitive from toxic clinical manifestations. The wide variation among published reports of the incidence of various hypersensitivity phenomena is illustrative of the unsatisfactory state of current reporting.

However, a recent, well-designed survey[2] sheds light on a serious aspect of drug hypersensitivity—the anaphylactoid reaction. Nearly a third of serious anaphylactoid reactions to antibiotics occurred in patients with allergic histories. Virtually all reactions were to parenterally administered penicillin. The tetracycline antibiotics and chloramphenicol were not implicated in anaphylactoid reactions in this study. It is not clear whether the higher incidence of penicillin-induced reactions is related to the more prolonged and extensive exposure of the population to this drug, or to the parenteral route of administration customarily employed in its use. That the severity of reaction may be related to dosage is suggested by the spontaneous desensitization observed with the slowly absorbed DBED penicillin.[1]

The foregoing facts as well as certain well-established principles of immunology must serve as a guide to rational antibiotic therapy in allergic patients in view of our limited knowledge of the risks entailed and the notorious unreliability of skin tests in assessing antibiotic hypersensitivity. In the allergic patient:

1. Antibiotics should be critically employed, and only when clearly indicated. Combined or multiple antibiotic therapy should be avoided.
2. Uninterrupted treatment should be maintained long enough to insure control of the infection.
3. The oral route of administration preferentially should be used when feasible.
4. Promiscuous use of topical antibiotic preparations is to be deplored.
5. Particularly in asthmatic patients, parenteral antibiotic therapy

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Presented as part of a Symposium on Antibiotics in the Allergic Patient, Southwest Allergy Forum, New Orleans, Louisiana, May 10, 1954.

From the Division of Infectious Disease, Department of Medicine, Tulane University School of Medicine.

should be attended by precautions for control of possible anaphylactoid reaction.

REFERENCES

1. Stollerman, G. H., and Rusoff, J. H.: Prophylaxis against group A streptococcal infections in rheumatic fever patients with new repository penicillin. J.A.M.A., 150:1571, 1952.
2. Welch H., Lewis, C. N., Kerlan, I., Putnam, L. E.: Acute anaphylactoid reactions attributable to penicillin. Antibiot. & Chemother., 3:891, 1953.

1430 Tulane Avenue

AMA REPORT ON INTERNSHIPS AND RESIDENCIES IN THE UNITED STATES

The Journal of the American Medical Association for September 25, 1954, contains the annual report of Internships and Residencies by the Council on Medical Education and Hospitals of the American Medical Association. In the report, which covers 115 pages, tables are presented giving statistical information on internships, showing a ten-year summary of approved hospitals, analyses of the number of internships by type of service, by type of hospital control, by bed capacity, and medical school affiliation, by census regions, a table on intern stipends, and a list of hospitals with highest autopsy rates. The second section of the report presents data on residencies, including tables on the number of residencies by type of hospital control, by bed capacity, and by medical specialties.

In the section devoted to Allergy, eighteen hospitals, with twenty-eight residencies and assistant residencies, were approved for one year of training by the Council and the Subspecialty Board for Allergy of the American Board of Internal Medicine. Following is the list of approved hospitals, together with their location, number of inpatients treated and number of outpatient visits, respectively:

		In	*Out*
Army Medical Center	Washington, D. C.	376	25,225
Veterans Administration Hospital	Long Beach, Calif.	362	5,572
Veterans Administration Hospital	Aspinwall, Penn.	150	19,125
Northwestern Univ. Medical Center (Incl. Veterans Admin. Research Hosp.)	Chicago, Illinois	25	3,400
University of Illinois Res. and Educ. Hospital	Chicago, Illinois	...	4,890
Massachusetts General Hospital	Boston, Mass.	...	7,316
University Hospital	Ann Arbor, Mich.	...	8,171
Mayo Foundation	Rochester, Minn.	...	.....
Jewish Hospital	Brooklyn, N. Y.	11	10,530
New York Hospital	New York, N. Y.	...	9,670
New York University-Bellevue Med. Center (Incl. University Hospital)	New York, N. Y. New York, N. Y.	12	6,445
Roosevelt Hospital	New York, N. Y.	222	38,721
Duke Hospital	Durham, N. C.	150	1,576
Temple University Hospital	Philadelphia, Penn.	...	3,801
Montefiori Hospital	Pittsburgh, Penn.	203	15,105
University of Virginia Hospital	Charlottesville, Va.	...	6,040
Medical College of Virginia, Hospital Division	Richmond, Va.	...	5,871

ROLE OF ALLERGY IN IMMUNOHEMATOLOGY

(Abstract)

CHARLES C. SPRAGUE, M.D.

New Orleans, Louisiana

THE ROLE of allergy in the rapidly expanding field of immunohematology is undoubtedly an important one. Almost certainly there are instances where allergy (exogenous and possibly endogenous) is at fault and never suspected. The classical papers of Ackroyd on the subject of Sedormid® purpura are noteworthy in this field. At present, blood dyscrasias are frequently diagnosed as auto-immune or idiopathic because of our lack of knowledge regarding their pathogenesis.

It is common knowledge that agents such as benzol derivatives, arsenicals, gold compounds and nitrogen mustard are capable of producing aplastic anemia, yet it is a rare individual who develops this condition when exposed to one of these. Undoubtedly, the bone marrow of some persons is more vulnerable than that of others, for reasons as yet unknown. Likewise, agranulocytosis can be produced regularly by administering certain toxic agents, such as x-ray, over a period of time, but on the other hand Amidopyrin in a single dose has been known to produce agranulocytosis in a hypersensitive individual. Acute hemolytic anemia may accompany certain infections in some patients, while other patients with the same infections show no evidence of increased hemolysis. Sulfonamide drugs are frequently administered with little thought of possible untoward effects, yet in a rare, susceptible patient they may produce a hemolytic syndrome. Sedormid, quinine, and Quinidine are some of the agents capable of producing a clinical syndrome indistinguishable from idiopathic thrombocytopenic purpura and only by careful questioning on the part of the physician may the true nature of the disorder be discovered. Schönlein-Henoch, nonthrombocytopenic purpura may be on an allergic basis in some instances, although the best evidence suggests that a preceding beta hemolytic streptoccocal infection is the commonest single etiologic factor that can be incriminated. Similarly, allergy may play a prominent role in other less well understood forms of vascular purpura.

Heretofore, there has been no attempt to study systematically blood dyscrasias arising from the administration of drugs. Recently, however, the Committee on Research of the Council on Pharmacy and Chemistry of the American Medical Association has enlisted the assistance of some seventy-two clinics throughout the United States to report all such in-

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From the Division of Hematology, Department of Medicine, Tulane University School of Medicine.

Presented at the Fifteenth Annual Meeting of the Southwest Allergy Forum, New Orleans, Louisiana, May 10, 1954.

stances that they observe. It is hoped that with their active participation, information regarding possible harmful effects of drugs can reach the practicing physician at a much earlier date than is now possible.

The physician must always be alert to the possibility of an allergic mechanism in "unusual" blood dyscrasias, which he labels idiopathic or auto-immune. Certainly a great deal remains to be learned regarding the pathogenesis of many of these disorders, but in some instances a strong suspicion and careful history may supply the answer.

1430 Tulane Avenue

ALLERGY KITS

The Raytheon Manufacturing Company of Waltham, Massachusetts, has available for distribution to physicians an allergy kit which should be of interest and help to allergists and general practitioners alike. It contains:

1. Several copies of a pamphlet published by the American Foundation for Allergic Diseases, entitled "Answers to Some Questions about Allergy and the Allergic Diseases," ideal for distribution to patients.

2. A copy of "The What, When, and Where of Hay Fever" prepared by the Botanical Research Department of Abbott Laboratories, which gives basic data on pollen and spores and is designed to assist in the diagnosis and treatment of hay fever. In graph form it shows the pollen seasons for various pollens for all states, and in chart form gives the pollen incidence (July through October) in pollen grains per cubic yard of air for various cities throughout the United States.

3. A bulletin entitled "Allergic Diseases in the United States" published by the American Foundation for Allergic Diseases. This is a comprehensive digest of current facts on the subject of allergy, and contains a full page bibliography.

4. A reprint of an article from the J.A.M.A. on "Pollen Prevalence and Pollen-free Areas" by Oren C. Durham, North Chicago, Illinois.

5. Three reports on hay fever and asthma, based on studies conducted by the Research Department of *Modern Medicine*.

6. A laboratory paper outlining the operating principles of the Raytheon Micronaire® Electrostatic Air Cleaner.

7. Several Micronaire folders giving complete information on this electrostatic air cleaner.

In Memoriam

CLARENCE S. BUCHER

It is with regret that we announce the sudden death on August 22, 1954, of Clarence S. Bucher, M.D., of Champaign, Illinois, at the age of seventy-two.

Born on November 26, 1881, in Whitehouse, Ohio, the son of the Rev. and Mrs. Benjamin Bucher, he was graduated from Loyola Medical School in Chicago in 1915. In the early 1920's he founded the Bucher Clinic in Champaign, Illinois, first medical clinic in the city, and this remained his office until the time of his death.

Dr. Bucher was instructor in allergy at the Julia F. Burnham School of Nursing, and was a member of the staff of Burnham City Hospital in Champaign. He was author of a number of medical articles, one of which, "The Prevention and Treatment of Some Psychoneurotic Conditions," is being published posthumously in the *Medical Times*. His book, "Nutrition and Diet in Allergy," appeared in 1953.

Dr. Bucher was a member of the American Medical Association, the Illinois State Medical Society, Champaign County Medical Society, the Radiological Society of North America, the Southwest Allergy Forum, and the International Association of Allergists. He was elected to Active Fellowship in the American College of Allergists in May, 1949.

An ardent fisherman, Dr. Bucher spent his vacations in northern Minnesota, relaxing with his family and pursuing his hobby.

His survivors include his wife, Sophia; his son, Richard C., and his daughter, Helen (Mrs. Owen H. Marshall), all of Champaign, as well as several sisters and brothers. To them, the members and officers of the College extend their sincere sympathy. Dr. Bucher was a conscientious, earnest, and valuable member of the College.

RATIONAL ANTIBIOTIC THERAPY

This is no ivory-tower discussion but one of considerable practical value. The unnecessary use of antibiotics can be materially reduced by distinguishing between virus and bacterial infections. Viral disorders are characterized by benignity, brevity, and prostration disproportionate to detectable signs of disease. Antibiotics are valueless in combating viral infections (except those due to rickettsiae), including 90 per cent of upper respiratory infections.—E. D. Kilbourne, *Gen. Pract.* 8(3):35, 1953.

News Items

INTERNATIONAL ROUND TABLE—FRIENDSHIP MEETING OF ALLERGOLOGISTS

(Preliminary Program)

The Dutch Allergologists have arranged an internationàl round table on the subject of "The Therapy of Bronchial Asthma" to be held at Utrecht, The Netherlands, May 26-28, 1955. Although no attempt is being made to hold another international congress, forty scientists from seventeen different countries have been invited to participate in discussions on research, examination, and therapy in bronchial asthma.

The Executive Committee in charge of the gathering consists of: Prof. Dr. H. W. Julius, Utrecht, Netherlands, and Dr. Fred W. Wittich, Minneapolis, Minnesota, Presidents of Honor; Dr. J. van Niekerk, Amsterdam, Netherlands, President; Dr. C. de Lind van Wijngaarden, The Hague, Netherlands, Vice President; Jhr. Dr. W. J. Quarles van Ufford, Utrecht, Netherlands, Secretary; and P. J. van der Werff, Amsterdam, Netherlands, Member. The tentative program includes the following papers: "Asthma Therapy in Old and Modern Times" by Dr. C. D. de Langen; "Physiopathology of the Asthma Attack and its Pharmacotherapy" by Dr. Bernard Halpern of Paris; "Specific Desensitization" by Drs. Egon Bruun of Copenhagen and P. J. van de Werff of Amsterdam; "House Dust Desensitization" by Dr. K. Maunsell of London; "Bacterial Vaccine Therapy" by Dr. A. W. Frankland of London and Prof. Jimenez Diaz; "Elimination Diet" by Dr. F. J. Farrerons of Barcelona and Dr. C. de Lind van Wijngaarden of The Hague: "Aspecific Desensitization" by Dr. Fred W. Wittich of Minneapolis, Minnesota; "Therapy by Family Education" by Dr. Eriksson-Lihr of Helsingfors; "Choice of a Profession and Change of Profession" by Dr. David Williams of Cardiff, Wales; "Children and Homes" by Dr. G. J. Huet of Bussum; "Climate Therapy" by Dr. W. Löffler of Zurich; "Asthma and Thermal Spas" by Prof. P. Sangiorgi; "Prevention Measures" by Dr. Bret Ratner of New York City and Dr. Wilken-Jensen of Copenhagen; "Psychological Therapy" by Dr. Harold Abramson of New York City and Dr. Stokvis; "Physiotherapy" by Dr. J. L. Livingstone of London and Dr. Quarles van Ufford of Utrecht; "Hormonal Therapy" by Dr. Pasteur Vallery-Radot of Paris, Dr. Bruce Pearson of London, and Dr. N. G. M. Orie of Groningen; "Antibiotic Therapy" by Dr. Jacques Duchaine of Brussels and Dr. J. Mulder of Leiden; "Chirurgical Therapy" by Dr. J. Swierenga of Utracht; "Treatment of Emphysema" by Dr. J. van Niekerk of Amsterdam" and "A Critical Review of the Statistics of Asthma Therapy" by Dr. K. Hansen of Lübeck.

The official language during the Round Table will be English, and the Proceedings of the Round Table will be published in English by Stenfert Kroese of Leiden, Netherlands.

A Definitive Program will be sent to all participants after final arrangements have been completed.

This tentative list of speakers and program indicates that this will be a most interesting and profitable meeting for workers in the field of asthmatology.

program will be given by experts who will present summaries of recent developments in their respective industries, including methods, costs, and results. One of the sessions will deal with "Sampling for Airborne Radioactivity." Tours of various plants to study control installations are planned.

SECTION ON ALLERGY—KINGS COUNTY MEDICAL SOCIETY

At the next meeting of the Section on Allergy of the Kings County Medical Society of Brooklyn, New York, to be held on November 30, 1954, Dr. Harold Lyons, Associate Professor of Medicine, College of Medicine, State University of New York, Brooklyn, New York, will present a paper on "Respiratory Function Tests and Aerosol Therapy in Respiratory Allergies." This paper will be discussed by Dr. Benjamin Burbank, Associate Clinical Professor of Medicine of the same faculty.

ALLERGY SECTION FORMED

A Section on Allergy has been formed in the Medical Society of the State of New York. Initiated by the Allergy Section of the Kings County Medical Society under the leadership of four Active Fellows of the College, Drs. Harry Markow, Harry Leibowitz, Emanual Schwartz, and Charles E. Spratt, and Dr. George A. Merrill, the resolution creating the section was passed by the House of Delegates at its annual meeting in May, 1954. The following officers were appointed:

Chairman .....Dr. Carl E. Arbesman, Buffalo, N. Y.
Vice Chairman .....Dr. William B. Sherman, New York City
Secretary .....Dr. Harry Leibowitz, Brooklyn, N. Y.

PHILADELPHIA ALLERGY SOCIETY

The fall meeting of the Philadelphia Allergy Society will be held on October 27, 1954, at the College of Physicians, Philadelphia, Pennsylvania. Dr. Stanley F. Hampton, Assistant Professor of Clinical Medicine, Washington University School of Medicine, will speak on "Causes and Treatment of Intrinsic Bronchial Asthma," followed by a discussion by Dr. Philip M. Gottlieb, Dr. Merle M. Miller, and Dr. Louis Tuft. In addition, three original papers on allergy will be presented by Dr. Arthur G. Baker, Dr. Charles S. Pennypacker, and Drs. Elliott L. Goodman and Edmund E. Ehrlich.

LABORATORY MANUALS AVAILABLE

Dr. Stephen D. Lockey still has available a few copies of the Manual of Office and Laboratory Procedures, which was used in his laboratory course at Miami Beach. These can be purchased for $4.00 each, plus twenty-five cents for postage, and all profits from such sales go into the treasury of the College. The books may be purchased direct from Dr. Lockey at 60 North West End Avenue, Lancaster, Pennsylvania.

THE AMERICAN COLLEGE OF ALLERGISTS

Eleventh Annual Instructional Course and Congress

Morrison Hotel, Chicago, Illinois

April 25-30, 1955

The *Eleventh Annual Instructional Course*, April 25-27, 1955, with Dr. Orval Withers, Chairman, and Dr. Morris A. Kaplan, Co-Chairman, will be held at the Morrison Hotel in Chicago. A tentative program has now been set up, but this, of course, is subject to change. Watch future issues of the ANNALS OF ALLERGY for important announcements and complete program.

As the Instructional Course is set up at the present time, Monday morning, April 25, will be devoted to the subject of FUNDAMENTALS OF ALLERGY, with lectures on Classification of Hypersensitive States, Principles of Immunology, Pathology and Physiology of Allergy, Diagnosis in Allergy, et cetera. The first luncheon speaker will discuss "Immunologic Aspects of Blood Dyscrasias." The afternoon session will be devoted to RESPIRATORY ALLERGY and will be comprised of lectures on Nasal Allergy; Pharmacology of Antihistaminic Drugs; Classification and Diagnostic Procedures in Bronchial Asthma; and Differential Diagnosis from Cardiovascular and other Pulmonary Conditions. Evening panel discussions will be held on Indications and Techniques of Various Pulmonary Pressure Machines, Inhalant Therapy in the Treatment of Bronchial Asthma, and Emphysema and Other Chest Conditions.

On Tuesday morning, April 26, the subject of RESPIRATORY ALLERGY will be continued, with lectures on the Management of Acute Attacks, Chronic Attacks, Smoker's Asthma, Postural Drainage, and Chemotherapy. The luncheon speaker will present a talk on "Chronic Emphysema and Its Management," and the afternoon session will be devoted to DERMATOLOGIC ALLERGY with papers on Electrolytes in the Treatment of Infantile Eczema, Pitfalls in the Diagnosis of Infantile Eczema, Symptomatic Treatment of Infantile Eczema, Common Causes of Contact Dermatitis, Modern Therapy of Atopic and Contact Dermatitis in Adults, Drug Allergy, Common Causes and Management of Urticaria and Angioneurotic Edema, and Allergic Purpura. Tuesday evening will be given over to a panel discussion on Office Management.

Wednesday morning, April 27, the subject will be NEWER CONCEPTS OF ALLERGIC CONDITIONS. Papers will deal with Pulmonary Function Tests, Cor Pulmonale, Endocrines, Pharmacology of Allergic Disorders, Newer Aspects of Psychotherapy in Allergic Practice, Management of the Pre-Allergic Child, and Special Problems in the Treatment of Bacterial Allergy. Miscellaneous topics will be considered on Wednesday afternoon, after a nationally-known speaker has presented a paper at the noon luncheon. The afternoon subjects will cover Allergy of the Alimentary Tract, Psychodynamics in Childhood Allergy, Immunologic Aspects of Idiopathic Acquired Hemolytic Anemia, Headache, Insect Allergy, Physical Allergy, Industrial Allergy, and other topics. The Wednesday evening session will consist of two panels: Mold Allergy and Questions, Please.

The General Scientific Session starts on Thursday morning, April 28, and papers of fifteen or twenty minutes' length will be presented during the entire day. A banquet with special entertainment is scheduled for the evening.

Friday morning will be devoted to PEDIATRIC ALLERGY, followed by two round table luncheons: one on Pediatric Allergy and the other on Ophthalmic and Otorhinolaryngologic Allergy. At the afternoon session the President's address will be given followed by the guest speaker, Dr. Robert Cooke, of New York City. There will be two sessions on Friday evening, one on Dermatologic Allergy and the other a Psychosomatic Workshop.

The Committee on Ophthalmic and Otorhinolaryngologic Allergy will be in charge of the Saturday morning session.

The deadline for papers for the Scientific Session is December 1, 1954. Please submit your papers to Dr. Lawrence J. Halpin, 808-810 Merchants National Bank Building, Cedar Rapids, Iowa, before that time.

NEWS ITEMS

AMERICAN PSYCHOSOMATIC SOCIETY

The American Pychosomatic Society will hold its Twelfth Annual Meeting at the Claridge Hotel in Atlantic City on Wednesday and Thursday, May 4 and 5, 1955. This meeting will be immediately preceded by those of the American Society for Clinical Investigation and the Association of American Physicians. It will be followed by the meeting of the American Psychoanalytic Association.

The Program Committee would like to receive titles and abstracts of papers for consideration for the program not later than December 1, 1954. Twenty minutes will be allotted for the reading of each paper. The Committee is interested especially in investigations in the theory and practice of psychosomatic medicine as applied to children and adults in all of the medical specialties, and in contributions in psychophysiology and ecology.

Abstracts for the Program Committee's consideration should be submitted in duplicate and sent to the chairman, Dr. Lawrence S. Kubie, 551 Madison Avenue, New York 22, N. Y.

OFFICERS ELECTED

The Chicago Society of Allergy has recently elected the following officers to serve for the year 1954-55: President, Max Samter, M.D.; President-Elect, Simon S. Rubin, M.D.; and Secretary-Treasurer, Norman J. Ehrlich, M.D.

ALLERGIST FEATURED

The September issue of *Coronet* contains a very human and interesting biographical sketch of Dr. Béla Schick, entitled "Always for the Children," by Carol Hughes. Dr. Schick became one of the first honorary fellows of the American College of Allergists in 1944. Although seventy-seven years of age, Dr. Schick refuses retirement and is at present Director of the Pediatric Department of Beth-El Hospital in New York. The article should be read to be appreciated.

NEWS OF COLLEGE MEMBERS

Dr. Sheldon C. Siegel, an Associate Fellow of the College, has recently been separated from service with the USAF Hospital at Lackland Air Force Base in San Antonio, Texas, and has moved into a new office in Los Angeles, California. Henceforth, his address will be: Children's Center, 5830 Overhill Drive, Los Angeles 43, California.

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Dr. Albert H. Unger has begun two years of service with the U. S. Army, and is to be stationed at William Beaumont Hospital, El Paso, Texas. He has set up an Allergy Clinic at that base for the personnel and dependents of that station, Fort Bliss, Biggs Air Force Base, and possibly other posts in the surrounding area. His current address is: Captain Albert H. Unger, 04022593, William Beaumont Army Hospital, Box 137, El Paso, Texas.

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Dr. Morris Scherago, Associate Fellow of the College, from the Department of Bacteriology of the University of Kentucky, Lexington, Kentucky, spent six weeks in Mexico recently at the invitation of the Institute of Tropical Diseases to make a study of an outbreak of a febrile disease in race horses. His study is continuing and promises to be an interesting one.

BOOK REVIEWS

A SOURCE-BOOK OF MEDICAL TERMS. Illustrated. Text by Edmund C. Jaeger, D.Sc., formerly Head, Department of Zoology, Riverside College, Riverside, California; foreword by Irvine H. Page, M.D., Director, Research Division, Cleveland Clinic Foundation, Cleveland, Ohio; illustrations by Lloyd Mason Smith and author. 165 pages. Springfield: Charles C Thomas, 1953. Price $5.50.

This is not a dictionary, but a volume that should prove highly useful to new students of medicine as well as to the "old grads"—a key to the meaning and significance of medical terms, which both are called upon to employ so frequently. The serious reader will encounter much information and knowledge in its pages, the casual reader considerable entertainment.

Apparently, no medical dictionary has attempted to do what this little source book has done. Here, the reader will find answers to his questions relative to the origin and literal meaning of words (simple and compound); their application in special cases; their history; and how they happen to be spelled as they are. The author has collected, in alphabetical sequence, the numerous word elements, combining forms, prefixes, and suffixes from which modern medical terms have been coined.

The introductory section of the book will be helpful, especially to those readers with no background in Greek and Latin grammar. There are tables on Latin nouns and forms of Latin adjectives, along with instructions on how to use the source book.

Two features, which add interest and pleasure to the reading of this book, are the pen and ink sketches illustrating the nature and associations of a word and the boxed-in entries containing facts of historical or other significance.

A good investment and an excellent item for the medical library of a man who wishes to use correctly the technical vocabulary which he must perforce employ in his daily routine! —*I.W.*

A FORMULARY FOR EXTERNAL THERAPY OF THE SKIN. By Chester N. Frazier, M.D., Edward Wigglesworth, Professor of Dermatology, Harvard Medical School and Chief of the Dermatological Service, Massachusetts General Hospital, Boston, Massachusetts, and Irvin H. Blank, Ph.D., Research Associate in Dermatology, Harvard Medical School and Massachusetts General Hospital, Boston, Massachusetts. Edited by Arthur C. Curtis, M.D., Chairman, Department of Dermatology and Syphilology, University of Michigan, Ann Arbor, Michigan. 118 pages. Springfield: Charles C Thomas, 1954. American Lecture Series. Price $3.25.

This monograph opens with an excellent prologue. The formulary was prepared originally to fill the requirements of the Massachusetts General Hospital and it is brief, objective and critical. There are eleven chapters dealing with evolution of the formulary, objectives of external therapy, some principles of treatment, cleaning the skin, including mechanism of the cleaning process, effect of the cleaning process on the skin, superfatted soaps, specific uses of soap substitutes, removal of keratinized epithelium and bacteria, and medicated soaps. Ointment vehicles are discussed as well as chemical and physical characteristics of the vehicles, hydrophobic oils, hydrophilic oils, emulsions, oil-powder vehicles, and performance of the vehicles after application to the cutaneous surface. Emollients and protectives, antipruritics, anti-infectives, antieczematous and antiseborrheic agents, and antiperspirants are evaluated, and there is a final chapter on formulary. There is a good index. This small treatise should be of invaluable aid to all practicing physicians.—*M.M.*

ACUTE PULMONARY EDEMA. By Mark D. Altschule, M.D., Assistant Professor of Medicine, Harvard Medical School, Boston, Massachusetts. Modern Medical Monograph series. 68 pages. New York: Grune and Stratton, 1954. Price $3.50.

This monograph is written for students of medicine, whether in school or in practice, and relates manifestations and treatment of acute pulmonary edema to what is known about certain physiologic phenomena. The first chapter deals with clinical manifestations, onset, interstitial phase, intra-alveolar phase, shock, terminal phase, angina pectoris and acute pulmonary edema, differential diagnosis, acute pulmonary edema and chronic cardiac decompensation, and prognosis. Basic physiologic considerations are taken up in the second chapter, including pulmonary fluid dynamics, and accumulation of fluid in the lungs.

The third chapter considers pathologic physiology, dyspnea, nocturnal occurrence of attacks, fever, shock, wheezing, spontaneous remissions, occurrence and pathogenesis, including coronary arteriosclerosis, mitral stenosis, aortic valvular disease, cardiac decompensation and a host of other conditions. Treatment is considered in the fourth chapter, and each chapter has a summary. A bibliography and index are included. This compact little book presents available knowledge in the form of a logically coherent system of ideas consistent with what is observable.—*M.M.*

HANDBOOK OF COSMETIC MATERIALS. Their Properties, Uses, and Toxic and Dermatologic Actions. By Leon Greenberg, Ph.D. and David Lester, Ph.D., Laboratory of Applied Physiology, Yale University, with a chapter on The Skin by Howard W. Haggard, M.D. 467 pages. New York and London: Interscience Publishers, 1954. Price $12.50.

The use of cosmetics in our modern society is increasing to such extent that almost every man and woman uses some cosmetic aids to enhance physical attractiveness or improve morale. The field of cosmetic materials has expanded in recent years to cover more than five thousand different and complex chemical compounds. The rapid increase in new compounds and their safety and desirability as constituents of cosmetics led the Toilet Goods Association to develop a basic reference work listing ingredients of these compounds and the known facts about them.

The handbook thus developed by the Yale University Laboratory of Applied Physiology was four years in the making, and contains a bibliography of over 2,700 items, a useful compilation of sources for research workers. Designed to facilitate the findings of information on the various compounds, each is listed alphabetically under the numerous terms by which it has been referred to in the literature, with the information concerning it listed only under the more familiar name or that believed to be correct. Information about each compound is organized under five headings: Formula (including collateral names); Properties; Uses; Toxic Action; and Dermatologic Action. References to the bibliography are included when pertinent.

Dr. Howard Haggard has written seventeen pages of text on the skin and its structure, hair, nails, sebaceous and sweat glands, influence of bodily condition upon the skin, absorption through the skin, penetration, dermatitis, and variations in susceptibility to irritation, all of which provide a basis for understanding of the action of the various substances with which the handbook deals.

To date there has been no single volume in which a large part of this basic information has been assembled. In addition to the cosmetic industry, this volume should be of considerable value to chemists, physicians, dermatologists, and allergists, in fact to all who need reliable information on the toxicity or allergenic qualities as well as the properties of cosmetic materials.—*V.E.S.*

BOOK REVIEWS

THE LABORATORY DIAGNOSIS OF LEPTOSPIROSIS. American Lecture Series. By J. W. Wolff, M.D., Professor of Tropical Hygiene, University of Wageningen; Bacteriologist, Institute of Tropical Hygiene and Geographical Pathology, Royal Tropical Institute, Amsterdam, The Netherlands. 106 pages, including index. Springfield, Illinois: Charles C Thomas, 1954. Price $3.75.

Since the discovery in 1916 of *Leptospira* as the causative organism of Weil's disease, knowledge of the infections caused by these spirochetes has increased considerably. The Institute of Tropical Hygiene and Geographical Pathology in Amsterdam was set up as a center of leptospiral research for the Netherlands, and most of the methods described in this book were developed by Schuffner and his co-workers there between 1923 and 1944. The author was one of Schuffner's early assistants in Amsterdam and later carried out investigations on leptospirosis in Indonesia.

Research in several countries has shown that leptospiral diseases occurred much more frequently than was formerly realized. Rodents, dogs, pigs, and bovines were found to be renal carriers of leptospirae, and in certain areas these animals were the chief source of human infections. Although cases of leptospirosis have now been detected in nearly every country of the world, our knowledge is far from complete; however, the co-operation between clinician, laboratory worker, and epidemiologist has shown results. International co-operation to promote comparison of laboratory techniques for leptospiral research has now been inaugurated by members of the Leptospira Subcommittee of the Nomenclature Committee of the International Association of Microbiologists.

This little book aims to give in a concise form practical suggestions for those who are not specialists in leptospiral research, and should be helpful to medical and veterinary laboratory workers interested in expanding this field of research. Its pages cover morphology, staining methods, antigenic structures of leptospira, and characteristics of type strains of leptospira, in addition to such diagnostic procedures as dark-field examination of blood, cerebrospinal fluid and urine, cultural procedures and media, animal inoculation, and serologic procedures (including agglutination-lysis and agglutinin-absorption tests).

The book contains a ten-page bibliography and an index.—*V.E.S.*

HEADACHE: DIAGNOSIS AND TREATMENT. Robert E. Ryan, B.S., M.D., M.S., F.A.C.S., Department of Otolaryngology, St. Louis University; Former Fellow of Mayo Clinic, Rochester, Minnesota; Associate Otolaryngologist, St. John's Hospital; Assistant Otolaryngologist, St. Louis University Group of Hospitals, St. Louis, Missouri; Diplomate, American Board of Otolaryngology; Fellow of American Academy of Ophthalmology and Otolaryngology. 338 pages. St. Louis: The C. V. Mosby Company, 1954. Price $6.50.

This very thorough analysis of the headache problem has grown out of the author's work at the Mayo Clinic with Dr. Bayard T. Horton and Dr. Henry L. Williams. There every variety of headache was studied, and in this handy reference work the results of this study are passed on in a brief, yet complete, form.

After dealing with the physiologic basis of head pain, the objectives of headache therapy, differential diagnosis of head pain, the importance of history taking, and the examination of the headache patient, Dr. Ryan deals separately with the various types of headaches, discussing each with respect to etiology, symptomatology, diagnosis, prognosis, and treatment, both symptomatic and prophylactic. Atypical as well as the average types of headaches are covered, and the treatment outlined in each case is the most efficient known at the present time.

Separate chapters deal with: histaminic cephalalgia; migraine; abdominal and ophthalmic migraine; tension headache; generalized vasodilating headache; psycho-

genic headache; nasal sinusitis headache; Sluder's syndrome headache; myalgia of the head; mixed type of headache; head pain of otological origin; acute meningitis; trigeminal neuralgia; gloss-pharyngeal neuralgia; temporal arteritis; brain tumor headache; brain abscess; subarachnoid hemorrhage; post-traumatic headache; subdural hematoma; lateral sinus thrombosis; alcoholic headache; hypoglycemic headache; cardiovascular renal headache; constipation headache; gynecological headache; allergic headache; oral cavity head pain; muscle tension headache; migraine in children; postspinal puncture headache; and ophthalmological head pain. Headaches due to a number of conditions are also reviewed: bone disease, blood abnormalities, intoxications (poisonings), cardiac diseases, diseases of endocrine glands, cervical pathology, cerebral pathology, infectious diseases of bacterial origin, diseases of virus origin, infectious diseases of rickettsial origin, diseases of mycotic origin, diseases of protozoan origin; and various other conditions associated with headache.

Some of Dr. Ryan's co-workers at St. Louis University have cooperated with him in this work. Dr. Joseph A. Hardy, director of the Department of Obstetrics and Gynecology, wrote the chapter on gynecological headaches; Dr. Leslie Drews of the Department of Ophthalmology prepared the chapter on ophthalmological head pain; Dr. John J. Hammond of the Department of Medicine cooperated with the author in the preparation of the chapter on cardiovascular renal headache; and Dr. R. Frank Palazzo of the Department of Neurosurgery co-authored the chapters on brain tumor and brain abscess headaches.

This well-written volume should be of interest and help to all members of the medical profession as it covers conditions applicable to all fields and disciplines in medicine.—*V.S.*

MANUAL OF THE NORTH AMERICAN SMUT FUNGI. George William Fischer, Professor of Plant Pathology and Chairman of the Department, State College of Washington, Pullman, Washington. 350 pages. New York: Ronald Press Company, 1953. Price $8.75.

This up-to-date handbook on the taxonomy of the smuts was written to enable persons with some botanical and mycological background to identify with reasonable certainty any of the species of smut fungi known to occur in North America.

Covering twenty-two genera, 276 species, and several varieties of smut fungi on species of 242 host genera, the manual contains a combination host index and key designed for the quickest possible species determination. In many instances species descriptions are based on personal study of type material.

The author has included details of morphology previously overlooked or not mentioned, and thus amplified descriptions are given for many species. Nomenclature conforms to the International Rules of Botanical Nomenclature.

References to biological features such as spore germination, life history, and control have not been included, as they are covered by the author's *The Smut Fungi,* and a later volume is planned dealing entirely with the biology of the smut fungi.

The book is divided into four sections: Introduction; Host Genus Index and Key to the Species of North American Smut Fungi; Key to the Genera of the North American Smut Fungi; and (descriptions of) North American Smut Fungi, covering Burrillia, Cintractia, Doassansia, Entyloma, Farysia, Melanopsichium, Mykosyrinx, Neovossia, Planetella, Schizonella, Sorosporium, Sphacelotheca, Testicularia, Thecaphora, Tilletia, Tolyposporella, Tolyposporium, Tracya, Tuburcinia, Urocystis, Ustacystis, and Ustilago.

Nearly all the species are illustrated in 136 half tones, and photographs are included of habit pictures of infected plants with insets showing the spores and other microscopic features.

Those physicians who apply allergy to their practice, particularly those residing in the great grain belt area of the middle and northwestern United States, western Canada, and along the Great Lakes where there is handling and storage of grain, encounter respiratory allergies undoubtedly caused or aggravated by grain smuts, as shown by the reviewer in researches published on allergy to grain smuts. This manual makes it easy to identify the grain smuts encountered in any locality on this continent.

A short bibliography and a complete index are included.—*F.W.W.*

PRACTICE OF ALLERGY. Third Edition. Warren T. Vaughan, M.D., Richmond, Virginia. Revised by J. Harvey Black, M.D., Dallas, Texas. 1164 pages. St. Louis, Missouri: C. V. Mosby Company, 1954. Price $21.00.

The contents of this new edition cover in an authoritative way the steps in the development of our present understanding of clinical allergy.

The book is quite a departure from the one Dr. Warren Vaughan originally wrote. In revising it, however, Dr. Black has maintained the format, style, and approach to the subject as the author originally wrote it. He has successfully made the many changes necessary when evaluating and bringing up to date the vast mass of accumulated material on the subject of allergy. It was necessary to rewrite many parts of the book, and the present authors have successfully interpolated the new material, making it conform to the old in the interest of smoother reading.

Only those references are included which are representative and accessible to the reader, yet in spite of this limitation the number is practically doubled over the second edition.

There are fifteen parts, composed of sixty-six chapters, covering the various steps in our present understanding of the practice of allergy, general characteristics of clinical allergy, physiology of allergy, allergic diagnosis, diagnosis and treatment of food allergy and food allergens, the role of pollens and pollinosis and other inhalant allergy, bacterial allergy, allergy due to fungi, diadermal allergy, anaphyactic shock and its treatment, drugs, contact allergy, pharmacology, and a number of chapters on the various allergic diseases. An excellent new chapter on pulmonary function studies has been added and the original chapter on vital capacity determination by Dr. James Holman has been retained. Changes have been made in the chapter on fungus allergy by Dr. J. H. Howell, and a section has been added on the treatment of poison ivy dermatitis, which should be very helpful. O. C. Durham has brought up to date the chapters on pollen counts and surveys, and they provide much more information than formerly, and are, of course, authoritative.

The book is illustrated with photographs and charts of all kinds.

No student of allergy should be without this complete, authoritative, and up-to-date textbook on allergy, and it is invaluable as a ready reference book for the specialist.—*F.W.W.*

PRIMER OF ALLERGY. A guidebook for those who must find their way through the mazes of this strange and tantalizing state. Fourth edition. Warren T. Vaughan, M.D., Richmond, Virginia. Revised by J. Harvey Black, M.D., Dallas, Texas. Illustrated by John P. Tillery. 191 pages. St. Louis, Missouri: C. V. Mosby Company, 1954. Price $4.25.

This most important primer, as revised by Dr. J. Harvey Black, is now in its fourth edition as the result of a large demand, strong evidence of the desire of the readers for such a clear, concise, authoritative, and informative handbook suitable for allergy patients of all ages. It adequately provides answers to the many questions which arise in the minds of those who suffer from allergic conditions.

More extensive changes are made in this edition than in the third revision, due to the accumulation of new knowledge to be passed on to the reader.

It is a book which any physician can unhesitatingly recommend to his allergy patients, and its perusal should result in greater cooperation on the part of the patients, as a consequence of his being better informed.

A chapter on drugs commonly used in allergic conditions has been added.

The illustrations are humorous and are drawn after a "military" style.—*F.W.W.*

OF PUBLISHING SCIENTIFIC PAPERS. By George E. Burch, M.D., F.A.C.P. Henderson Professor of Medicine, Tulane University School of Medicine, New Orleans, Louisiana. 40 pages. New York: Grune & Stratton, 1954. Price $2.75.

This little book in a plastic spiral binding contains an essay presented at the Central Society for Clinical Research in Chicago on October 30, 1953.

Cleverly illustrated with delightful drawings, the author discusses scientific papers from the standpoint of the investigator-author, reader, benefactor-administrator, editor and editorial board, publisher, and lay press, telling what is done and what is not done.

Highly critical of the practice of requiring papers for qualification for membership in certain societies, to fill journals, and to satisfy the demands of certain readers, the author feels that improvement in the quality of scientific papers can come only by demanding the highest integrity and performance on the part of all involved in such writing, from the author through to the publisher. He makes no concrete suggestions for improvement, but expresses the hope that the essay will provoke discussion and self-criticism.—*V.E.S.*

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1. Segal, M. S., et al.: Ann. Allergy 9: 782-809, 1951.

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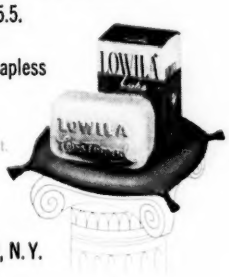

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